FIG. 1

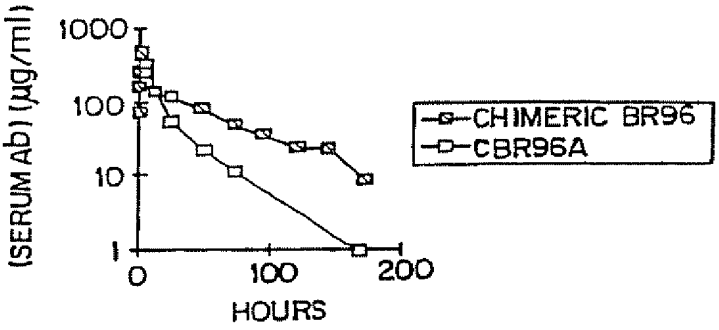

(SERUM Ab) (µg/ml)
1000
100
10
1
0
100
200
HOURS
CHIMERIC BR96
CBR96A

FIG. 2

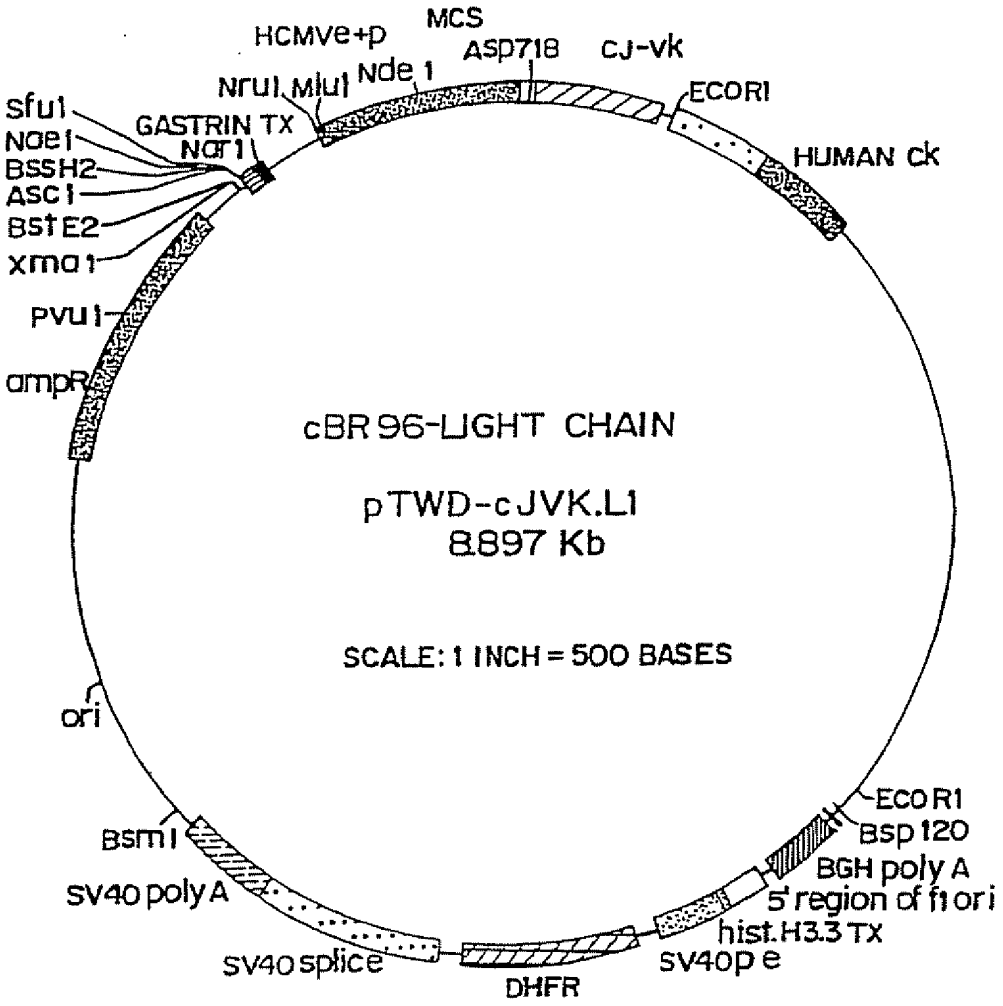

MCS
HCMVe+p
ASP718
CJ-VK
Nde 1
Nru1 Mlu1
ECORI
Sfu1
GASTRIN TX
Not1
Not1
BssH2
Asc1
BstE2
xma1
HUMAN Ck
Pvu1
ampR
cBR96-LIGHT CHAIN
pTWD-cJVK.L1
8.897 Kb
SCALE: 1 INCH = 500 BASES
ori
ECO R1
Bsm1
Bsp 120
BGH poly A
SV40 poly A
5' region of f1 ori
hist.H3.3 TX
SV40 splice
SV40 p e
DHFR

FIG. 3

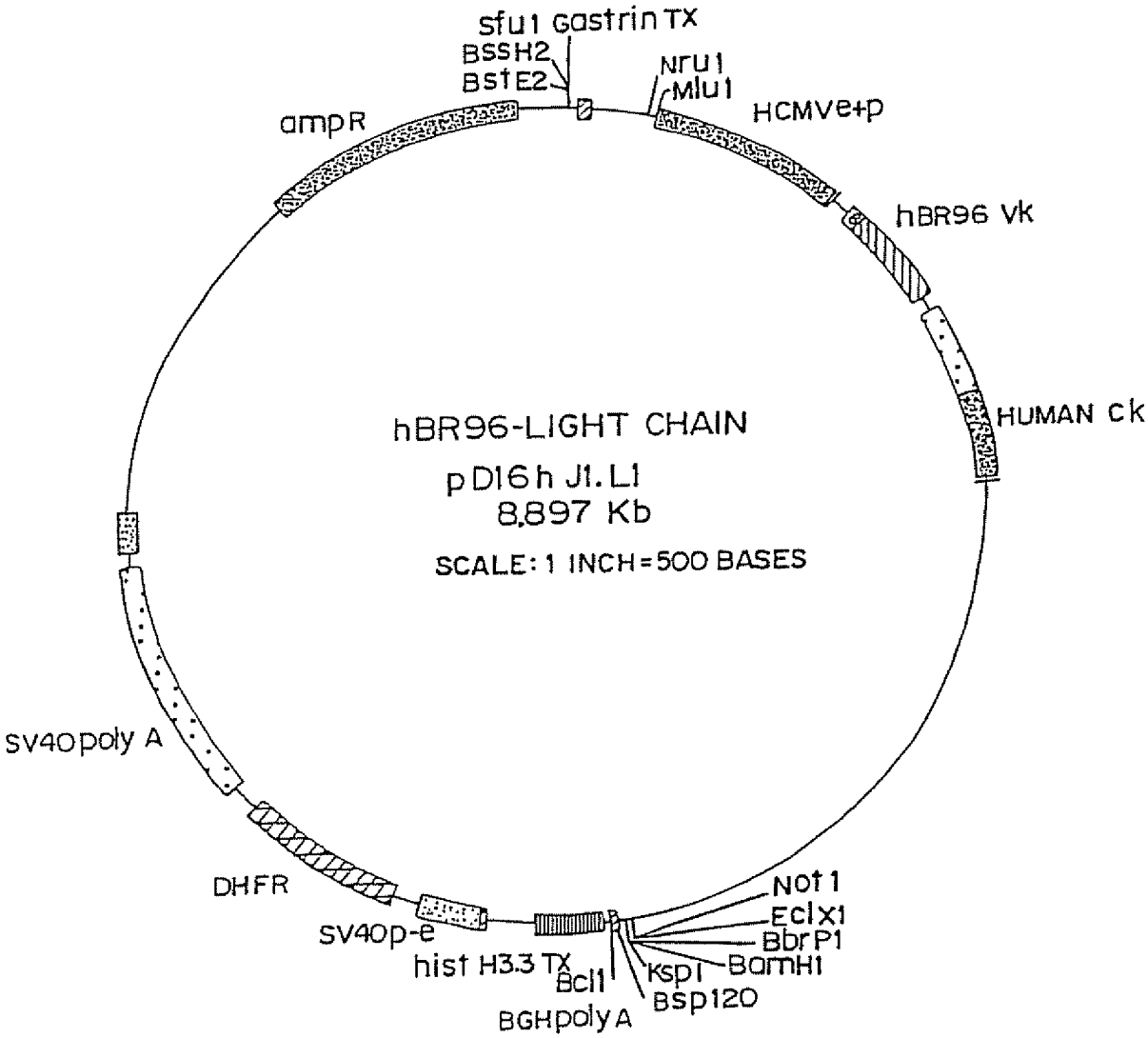

sfu1 Gastrin TX
BSSH2
BstE2
Nru1
Mlu1
HCMVe+p
hBR96 Vk
HUMAN ck
ampR
hBR96-LIGHT CHAIN
pD16h J1.L1
8.897 Kb
SCALE: 1 INCH=500 BASES
sv40poly A
DHFR
sv40p-e
hist H3.3 TX
Bcl1
BGHpoly A
Not 1
EclX1
BbrP1
Kspl
BamH1
Bsp120

FIG. 4

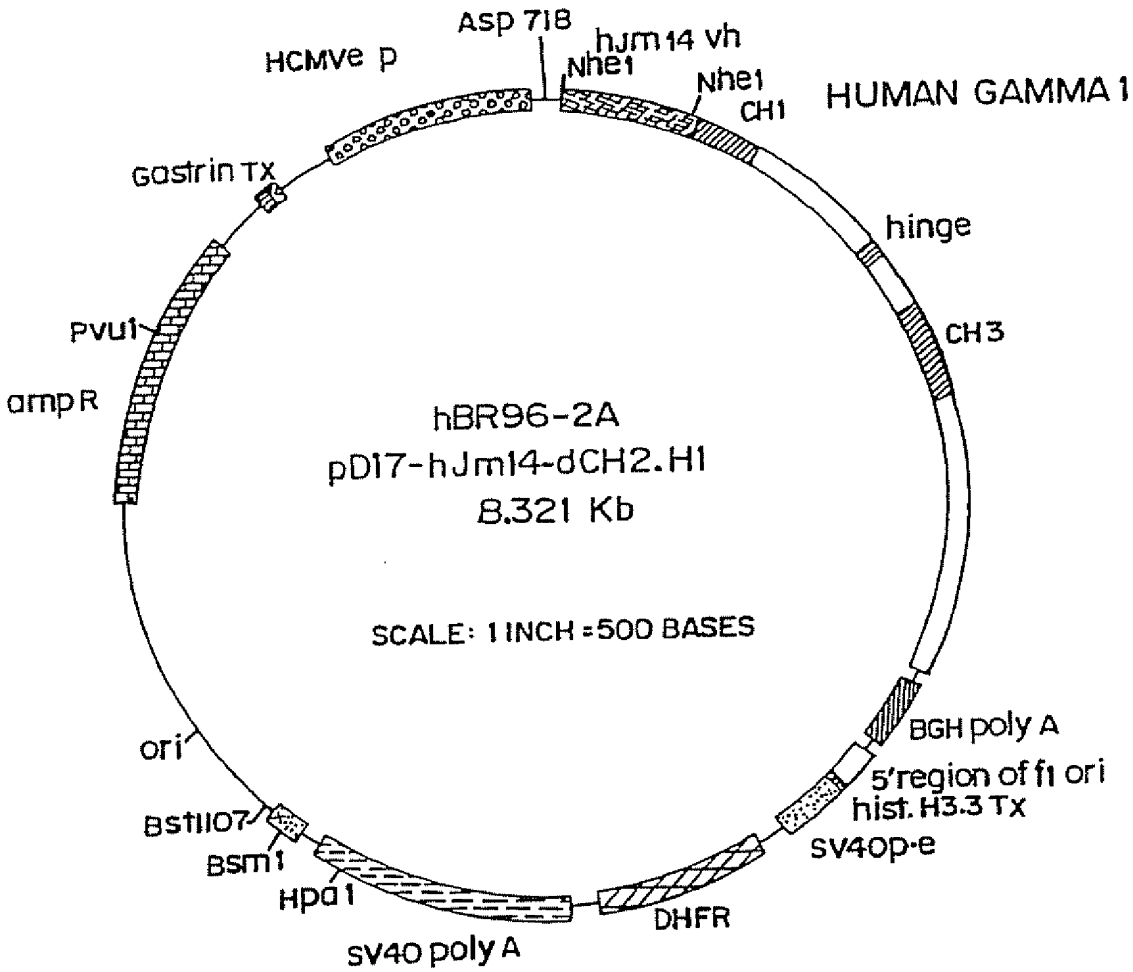

Asp 718
hJm14 vh
Nhe1
Nhe1
CH1
HUMAN GAMMA 1
HCMVe p
Gastrin TX
hinge
CH3
Pvu1
ampR
hBR96-2A
pD17-hJm14-dCH2.H1
8.321 Kb
SCALE: 1 INCH =500 BASES
BGH poly A
5'region of f1 ori
hist. H3.3 Tx
SV40p-e
ori
BstII07
Bsm1
Hpa1
DHFR
SV40 poly A

FIG. 5

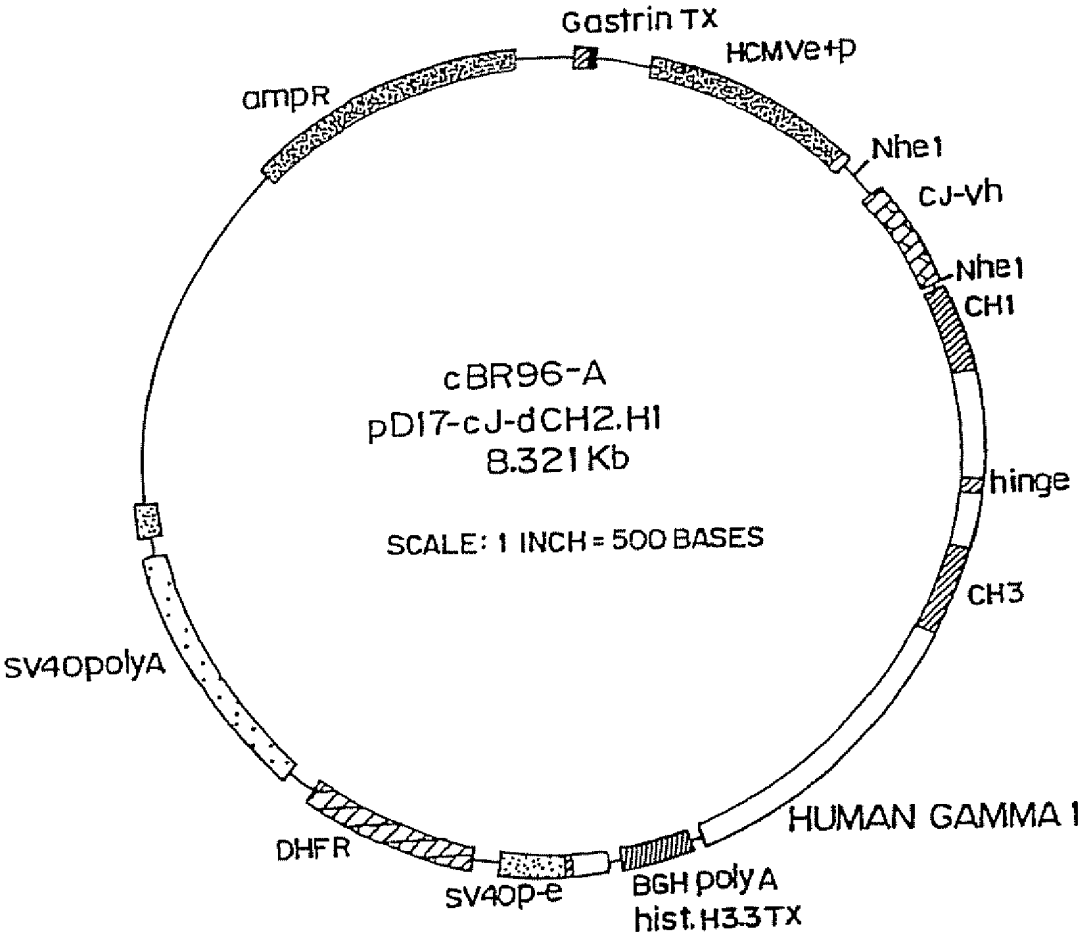

Gastrin TX
HCMVe+p
Nhe1
cJ-vh
Nhe1
CH1
hinge
CH3
HUMAN GAMMA 1
BGH poly A
hist. H3.3TX
sv40p-e
DHFR
sv40polyA
ampR
cBR96-A
pD17-cJ-dCH2.H1
8.321 Kb
SCALE: 1 INCH = 500 BASES

FIG. 6

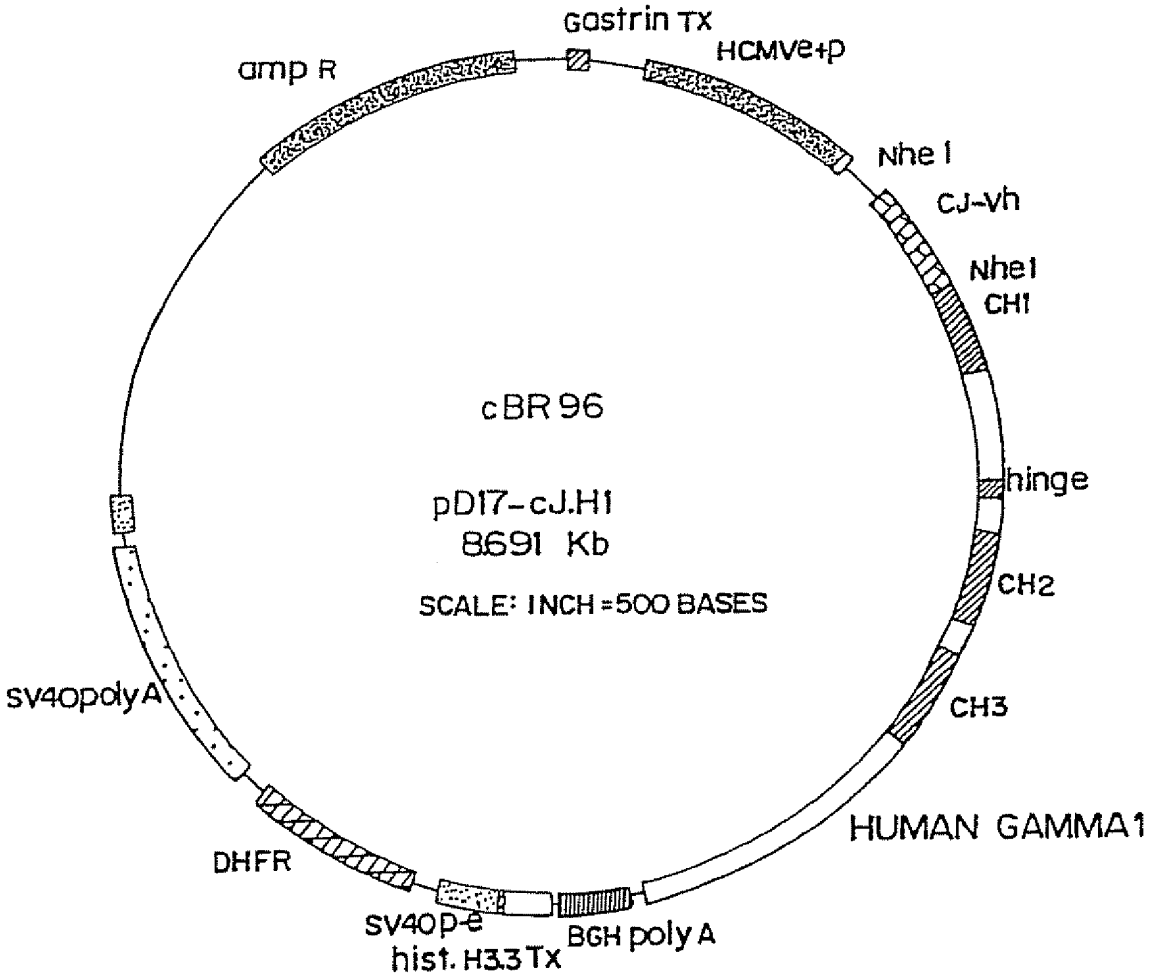

Gastrin TX
HCMVe+p
amp R
Nhe I
CJ-Vh
Nhe I
CH1
cBR 96
pD17-cJ.H1
8.691 Kb
SCALE: INCH =500 BASES
hinge
CH2
CH3
HUMAN GAMMA1
SV40polyA
DHFR
SV40p-e
hist. H3.3 Tx
BGH poly A

FIG. 7

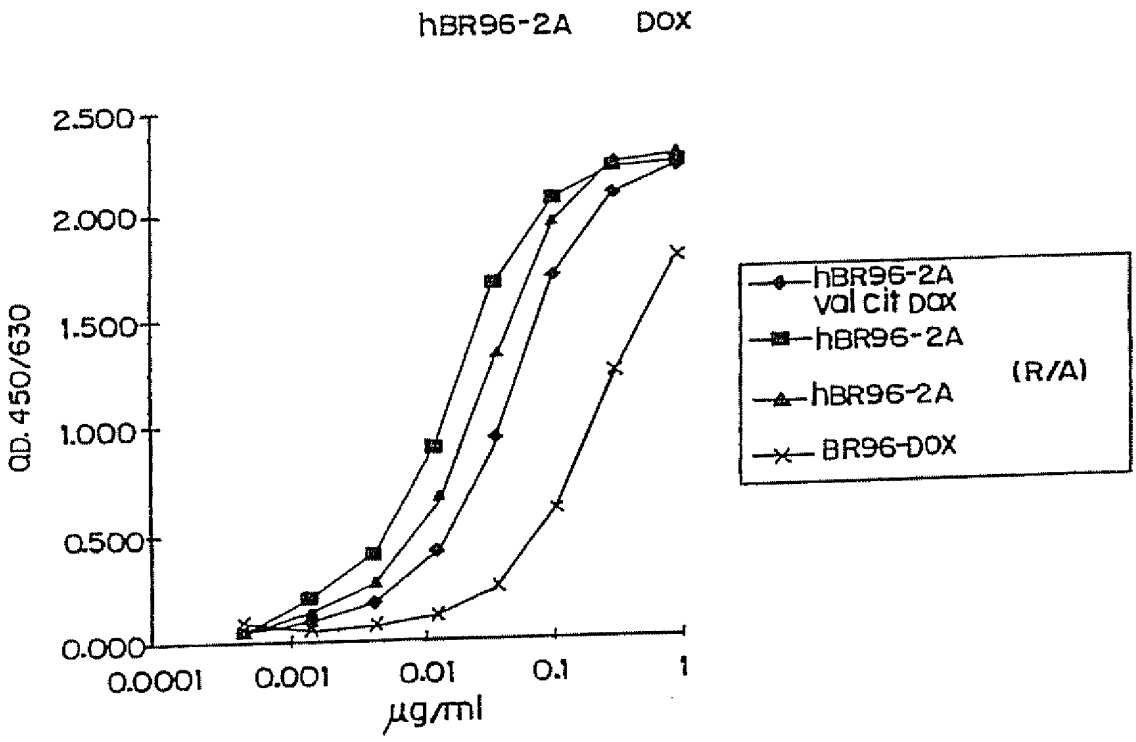

hBR96-2A DOX
2.500
2.000
1.500
1.000
0.500
0.000
O.D. 450/630
0.0001
0.001
0.01
0.1
1
µg/ml
hBR96-2A val cit DOX
hBR96-2A
hBR96-2A
BR96-DOX
(R/A)

FIG. 8

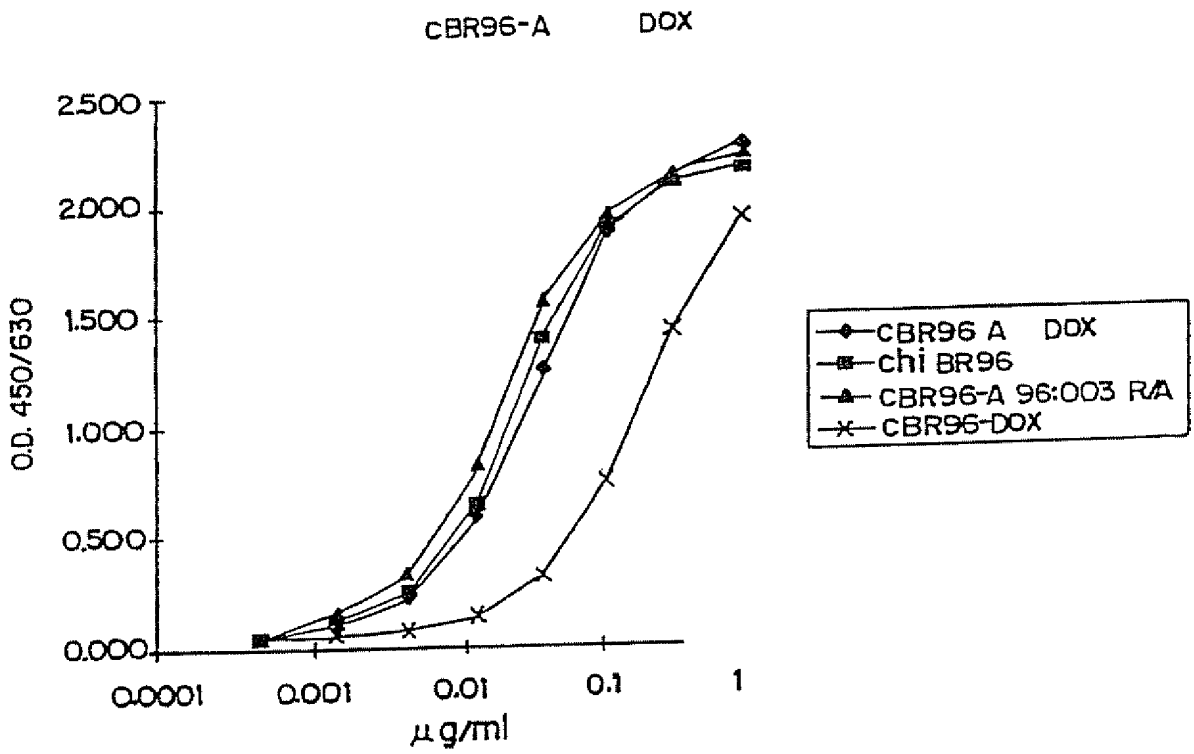

cBR96-A DOX
2.500
2.000
1.500
1.000
0.500
0.000
O.D. 450/630
0.0001
0.001
0.01
0.1
1
µg/ml
cBR96 A DOX
chi BR96
cBR96-A 96:003 R/A
cBR96-DOX

FIG. 9A

A-HINGE + CH2 + CH3 DOMAINS WERE REMOVED FROM BR96 IgG1 CONSTRUCT BY E.CO.47-III RESTRICTION DIGESTION.

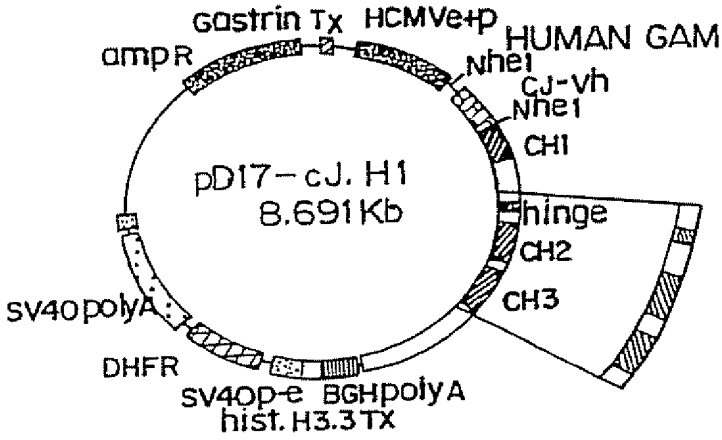


FIG. 9B

B-HINGE+CH3 DOMAINS AMPLIFIED BY PCR FROM L6 IgG1 CONSTRUCT LACKING THE CH2 DOMAIN.

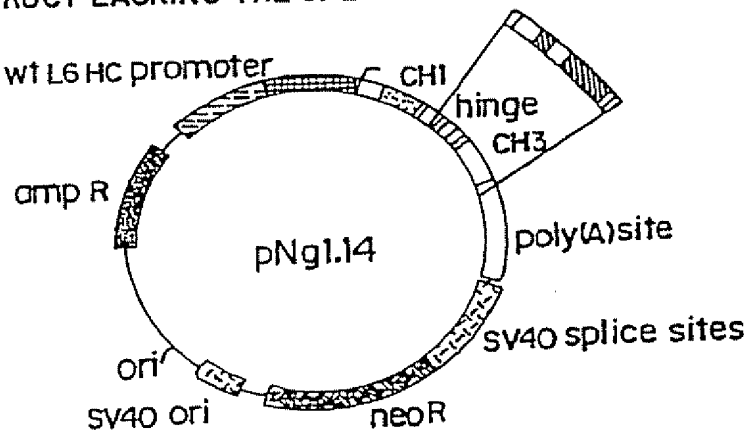
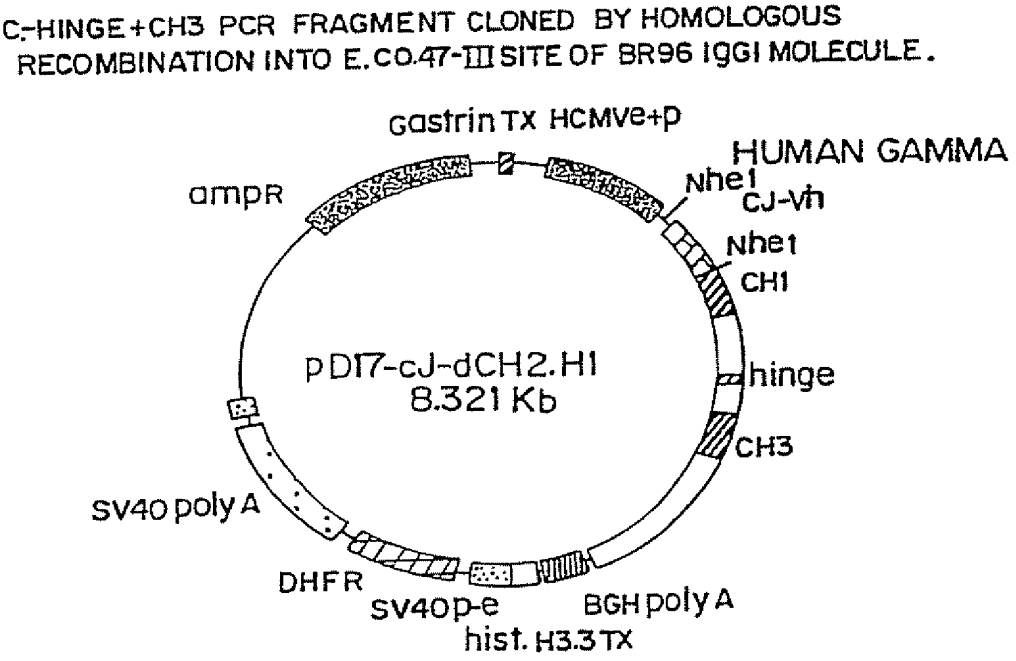


FIG. 9C


C-HINGE+CH3 PCR FRAGMENT CLONED BY HOMOLOGOUS RECOMBINATION INTO E.CO.47-III SITE OF BR96 IGG1 MOLECULE.
Gastrin TX HCMVe+p
HUMAN GAMMA
ampR
Nhe1
CJ-Vh
Nhe1
CH1
pD17-cJ-dCH2.H1
8.321 Kb
hinge
CH3
SV40 poly A
DHFR
SV40p-e
BGH poly A
hist. H3.3 TX

1.- INTRODUCTION OF MUTATIONS BY SITE DIRECTED MUTAGENESIS ON DOUBLE-STRANDED PLASMID DNA.

FIG. 10A

A.- MUTATIONS INTRODUCED INTO SYNTHETIC OLIGONUCLEOTIDES USED FOR THE PCR AMPLIFICATION OF CH2 DOMAIN

FIG. 10B

B.- PLASMID DNA LINEARIZED INSIDE CH2 DOMAIN AND CO-TRANSFORMED WITH PCR FRAGMENT INTO COMPETENT DH5α

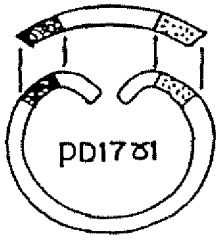


FIG. 10C

C.- CLONING MEDIATED BY HOMOLOGOUS RECOMBINATION YIELDS TRANSFORMANTS HARBOURING RECOMBINANT PLASMIDS.

FIG. 11

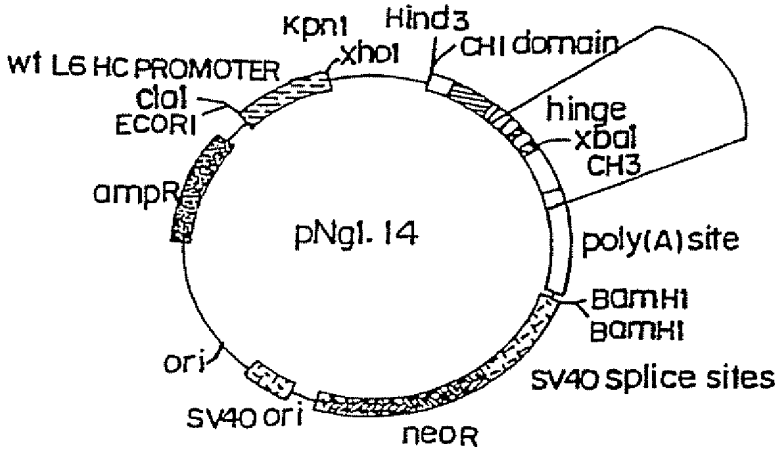


FIG. 12

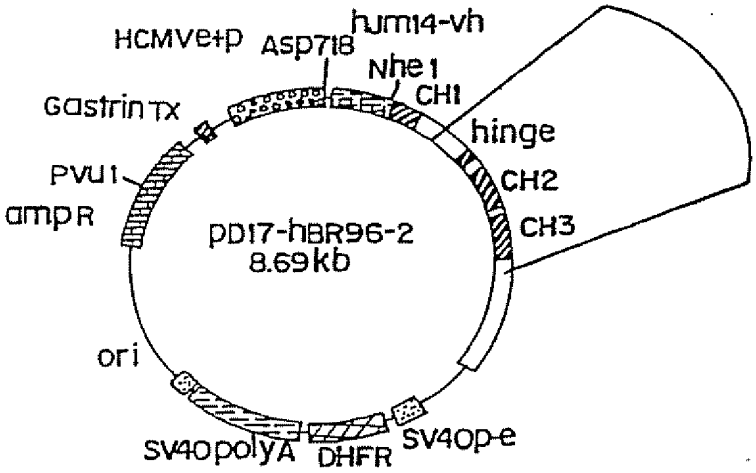


FIG. 13

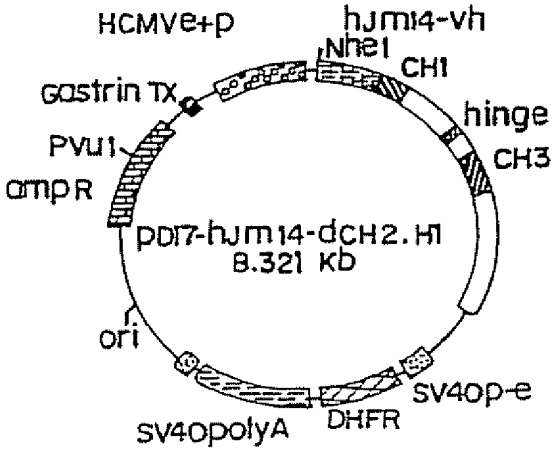


FIG. 14A
Primary Sequence = SEQ ID NO:10
Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                                                
```

FIG. 14B

Primary Sequence = SEQ ID NO:10

Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                                                
```

FIG. 14C

Primary Sequence = SEQ ID NO:10

Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                1810        1820        1830        1840        1850        1860        1870        1880        1890
GGCCAGCACA GGGAGGGAGG GTGTCTGCTG GAAGCCAGGC TCAGCGCTCC TGCCTGGACG CATCCCGGCT ATGCAGCCCC AGTCCAGGGC
CCGGTCGTGT CCCTCCCTCC CACAGACGAC CTTCGGTCCG AGTCGCGAGG ACGGACCTGC GTAGGGCCGA TACGTCGGGG TCAGGTCCCG

                1900        1910        1920        1930        1940        1950        1960        1970        1980
AGCAAGGCAG GCCCCGTCTG CCTCTTCACC CGGAGGCCTC TGCCCGCCCC ACTCATGCTC AGGGAGAGGG TCTTCTGGCT TTTTCCCCAG
TCGTTCCGTC CGGGGCAGAC GGAGAAGTGG GCCTCCGGAG ACGGGCGGGG TGAGTACGAG TCCCTCTCCC AGAAGACCGA AAAAGGGGTC

                1990        2000        2010        2020        2030        2040        2050        2060        2070
GCTCTGGGCA GGCACAGGCT AGGTGCCCCT AACCCAGGCC CTGCACACAA AGGGGCAGGT GCTGGGCTCA GACCTGCCAA GAGCCATATC
CGAGACCCGT CCGTGTCCGA TCCACGGGGA TTGGGTCCGG GACGTGTGTT TCCCCGTCCA CGACCCGAGT CTGGACGGTT CTCGGTATAG

                2080        2090        2100        2110        2120        2130        2140        2150        2160
CGGGAGGACC CTGCCCCTGA CCTAAGCCCA CCCCAAAGGC CAAACTCTCC ACTCCCTCAG CTCGGACACC TTCTCTCCTC CCAGATTCCA
GCCCTCCTGG GACGGGGACT GGATTCGGGT GGGGTTTCCG GTTTGAGAGG TGAGGGAGTC GAGCCTGTGG AAGAGAGGAG GGTCTAAGGT

                2170        2180        2190        2200        2210        2220        2230        2240        2250
GTAACTCCCA ATCTTCTCTC TGCAGAGCCC AAATCTTGTG ACAAAACTCA CACATGCCCA CCGTGCCCAG GTAAGCCAGC CCAGGCCTCG
CATTGAGGGT TAGAAGAGAG ACGTCTCGGG TTTAGAACAC TGTTTTGAGT GTGTACGGGT GGCACGGGTC CATTCGGTCG GGTCCGGAGC

                2260        2270        2280        2290        2300        2310        2320        2330        2340
CCCTCCAGCT CAAGGCGGGA CAGGTGCCCT AGAGTAGCCT GCATCCAGGG ACACACCACG TGGGTACCAA CATGTCCGGA GCCACATGGA
GGGAGGTCGA GTTCCGCCCT GTCCACGGGA TCTCATCGGA CGTAGGTCCC TGTGTGGTGC ACCCATGGTT GTACAGGCCT CGGTGTACCT

                2350        2360        2370        2380        2390        2400        2410        2420        2430
CAGAGGCCGG CTCGGCCCAC CCTCTGCCCT GAGAGTGACC GCTGTACCAA CCTCTGTCCC TACAGGGCAG CCCCGAGAAC CACAGGTGTA
GTCTCCGGCC GAGCCGGGTG GGAGACGGGA CTCTCACTGG CGACATGGTT GGAGACAGGG ATGTCCCGTC GGGGCTCTTG GTGTCCACAT

                2440        2450        2460        2470        2480        2490        2500        2510        2520
CACCCTGCCC CCATCCCGGG ATGAGCTGAC CAAGAACCAG GTCAGCCTGA CCTGCCTGGT CAAAGGCTTC TATCCCAGCG ACATCGCCGT
GTGGGACGGG GGTAGGGCCC TACTCGACTG GTTCTTGGTC CAGTCGGACT GGACGGACCA GTTTCCGAAG ATAGGGTCGC TGTAGCGGCA

                2530        2540        2550        2560        2570        2580        2590        2600        2610
GGAGTGGGAG AGCAATGGGC AGCCGGAGAA CAACTACAAG ACCACGCCTC CCGTGCTGGA CTCCGACGGC TCCTTCTTCC TCTACAGCAA
CCTCACCCTC TCGTTACCCG TCGGCCTCTT GTTGATGTTC TGGTGCGGAG GGCACGACCT GAGGCTGCCG AGGAAGAAGG AGATGTCGTT

                2620        2630        2640        2650        2660        2670        2680        2690        2700
GCTCACCGTG GACAAGAGCA GGTGGCAGCA GGGGAACGTC TTCTCATGCT CCGTGATGCA TGAGGCTCTG CACAACCACT ACACGCAGAA
CGAGTGGCAC CTGTTCTCGT CCACCGTCGT CCCCTTGCAG AAGAGTACGA GGCACTACGT ACTCCGAGAC GTGTTGGTGA TGTGCGTCTT
```

FIG. 14D

Primary Sequence = SEQ ID NO:10

Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                                                
```

FIG. 14E

Primary Sequence = SEQ ID NO:10

Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
3610       3620       3630       3640       3650       3660       3670       3680       3690
CCAGCCCTCC TCTCACAAGG GTGCCCCTGC AGCCGCCACA CACACACAGG GGATCACACA CCACGTCACG TCCCTGGCCC TGGCCCACTT
GGTCGGGAGG AGAGTGTTCC CACGGGGACG TCGGCGGTGT GTGTGTGTCC CCTAGTGTGT GGTGCAGTGC AGGGACCGGG ACCGGGTGAA

3700       3710       3720       3730       3740       3750       3760       3770       3780
CCCAGTGCCG CCCTTCCCTG CAGGACGGAT CAGCCTCGAC TGTGCCTTCT AGTTGCCAGC CATCTGTTGT TTGCCCCTCC CCCGTGCCTT
GGGTCACGGC GGGAAGGGAC GTCCTGCCTA GTCGGAGCTG ACACGGAAGA TCAACGGTCG GTAGACAACA AACGGGGAGG GGGCACGGAA

3790       3800       3810       3820       3830       3840       3850       3860       3870
CCTTGACCCT GGAAGGTGCC ACTCCCACTG TCCTTTCCTA ATAAAATGAG GAAATTGCAT CGCATTGTCT GAGTAGGTGT CATTCTATTC
GGAACTGGGA CCTTCCACGG TGAGGGTGAC AGGAAAGGAT TATTTTACTC CTTTAACGTA GCGTAACAGA CTCATCCACA GTAAGATAAG

3880       3890       3900       3910       3920       3930       3940       3950       3960
TGGGGGGTGG GGTGGGGCAG GACAGCAAGG GGGAGGATTG GGAAGACAAT AGCAGGCATG CTGGGGATGC GGTGGGCTCT ATGGCTTCTG
ACCCCCCACC CCACCCCGTC CTGTCGTTCC CCCTCCTAAC CCTTCTGTTA TCGTCCGTAC GACCCCTACG CCACCCGAGA TACCGAAGAC

3970       3980       3990       4000       4010       4020       4030       4040       4050
AGGCGGAAAG AACCAGCTGG GGCTCTAGGG GGTATCCCCA CGCGCCCTGT AGCGGCGCAT TAAGCGCGGC GGGTGTGGTG GTTACGCGCA
TCCGCCTTTC TTGGTCGACC CCGAGATCCC CCATAGGGGT GCGCGGGACA TCGCCGCGTA ATTCGCGCCG CCCACACCAC CAATGCGCGT

4060       4070       4080       4090       4100       4110       4120       4130       4140
GCGTGACCGC TACACTTGCC AGCGCCCTAG CGCCCGCTCC TTTCGCTTTC TTCCCTTCCT TTCTCGCCAC GTTCGCCGGG CCTCTCAAAA
CGCACTGGCG ATGTGAACGG TCGCGGGATC GCGGGCGAGG AAAGCGAAAG AAGGGAAGGA AAGAGCGGTG CAAGCGGCCC GGAGAGTTTT

4150       4160       4170       4180       4190       4200       4210       4220       4230
AAGGGAAAAA AAGCATGCAT CTCAATTAGT CAGCAACCAT AGTCCCGCCC CTAACTCCGC CCATCCCGCC CCTAACTCCG CCCAGTTCCG
TTCCCTTTTT TTCGTACGTA GAGTTAATCA GTCGTTGGTA TCAGGGCGGG GATTGAGGCG GGTAGGGCGG GGATTGAGGC GGGTCAAGGC

4240       4250       4260       4270       4280       4290       4300       4310       4320
CCCATTCTCC GCCCCATGGC TGACTAATTT TTTTTATTTA TGCAGAGGCC GAGGCCGCCT CGGCCTCTGA GCTATTCCAG AAGTAGTGAG
GGGTAAGAGG CGGGGTACCG ACTGATTAAA AAAAATAAAT ACGTCTCCGG CTCCGGCGGA GCCGGAGACT CGATAAGGTC TTCATCACTC

4330       4340       4350       4360       4370       4380       4390       4400       4410
GAGGCTTTTT TGGAGGCCTA GGCTTTTGCA AAAAGCTTGG ACAGCTCAGG GCTGCGATTT CGCGCCAAAC TTGACGGCAA TCCTAGCGTG
CTCCGAAAAA ACCTCCGGAT CCGAAAACGT TTTTCGAACC TGTCGAGTCC CGACGCTAAA GCGCGGTTTG AACTGCCGTT AGGATCGCAC

4420       4430       4440       4450       4460       4470       4480       4490       4500
AAGGCTGGTA GGATTTTATC CCCGCTGCCA TCATGGTTCG ACCATTGAAC TGCATCGTCG CCGTGTCCCA AAATATGGGG ATTGGCAAGA
TTCCGACCAT CCTAAAATAG GGGCGACGGT AGTACCAAGC TGGTAACTTG ACGTAGCAGC GGCACAGGGT TTTATACCCC TAACCGTTCT
```

FIG. 14F
Primary Sequence = SEQ ID NO:10
Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                                                
```

FIG. 14G
Primary Sequence = SEQ ID NO:10
Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                                                
```

FIG. 14H

Primary Sequence = SEQ ID NO:10

Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                                                
```

FIG. 14I

Primary Sequence = SEQ ID NO:10

Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
                                                
```

FIG. 14J
Primary Sequence = SEQ ID NO:10
Complementary Sequence = SEQ ID NO:28

pD17-cJ-dCH2.H1

```
      8110       8120       8130       8140       8150       8160       8170       8180       8190
CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG GGAATAAGGG CGACACGGAA ATGTTGAATA CTCATACTCT
GGTCGCAAAG ACCCACTCGT TTTTGTCCTT CCGTTTTACG GCGTTTTTTC CCTTATTCCC GCTGTGCCTT TACAACTTAT GAGTATGAGA

      8200       8210       8220       8230       8240       8250       8260       8270       8280
TCCTTTTTCA ATATTATTGA AGCATTTATC AGGGTTATTG TCTCATGAGC GGATACATAT TTGAATGTAT TTAGAAAAAT AAACAAATAG
AGGAAAAAGT TATAATAACT TCGTAAATAG TCCCAATAAC AGAGTACTCG CCTATGTATA AACTTACATA AATCTTTTTA TTTGTTTATC

      8290       8300       8310       8320       8330
GGGTTCCGCG CACATTTCCC CGAAAAGTGC CACCTGACGT C
CCCAAGGCGC GTGTAAAGGG GCTTTTCACG GTGGACTGCA G
```

FIG. 15

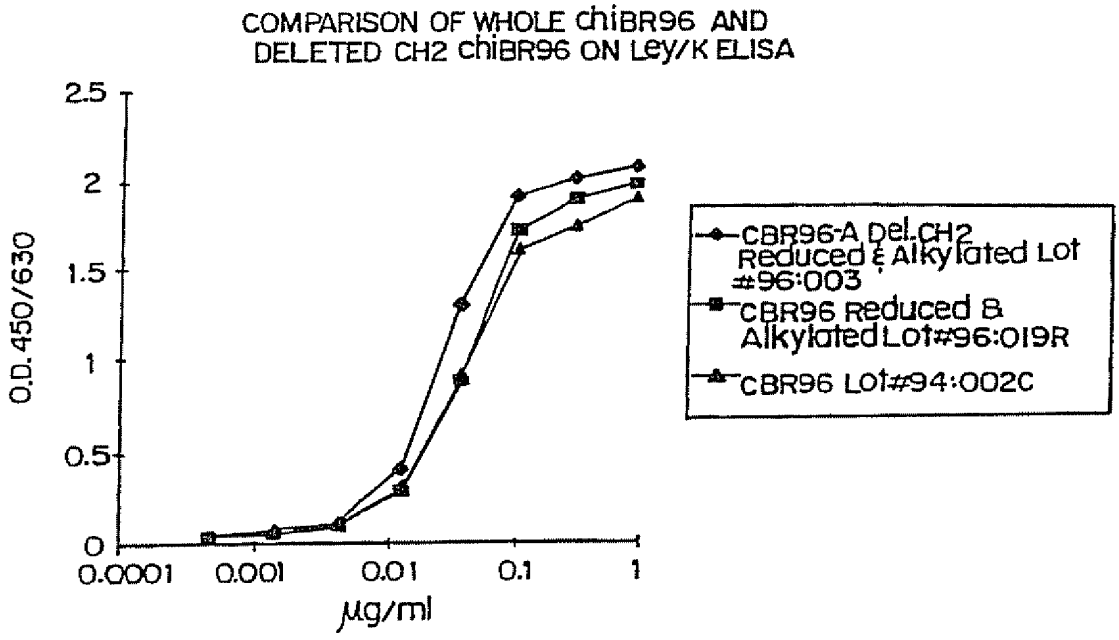

COMPARISON OF WHOLE chiBR96 AND
DELETED CH2 chiBR96 ON Ley/K ELISA
2.5
2
1.5
1
0.5
0
O.D. 450/630
0.0001
0.001
0.01
0.1
1
µg/ml
CBR96-A Del.CH2 Reduced & Alkylated Lot #96:003
CBR96 Reduced & Alkylated Lot#96:019R
CBR96 Lot#94:002C

FIG. 16

hBR96-2B:L235 to A235 and G237 to A237

hBR96-2C:E318 to S318, K320 to S320, and K322 to S322

hBR96-2D:P331 to A331

hBR96-2E:L235 to A235, G237 to A237, E318 to S318, K320 to S320, and K322 to S322

hBR96-2F:L235 to A235, G237 to A237, and P331 to A331

hBR96-2G:E318 to S318, K320 to S320, K322 to S322, and P331 to A331

hBR96-2H: L235 to A235, G237 to A237, E318 to S318, K320 to S320, K322 to S322, and P331 to A331

FIG. 17

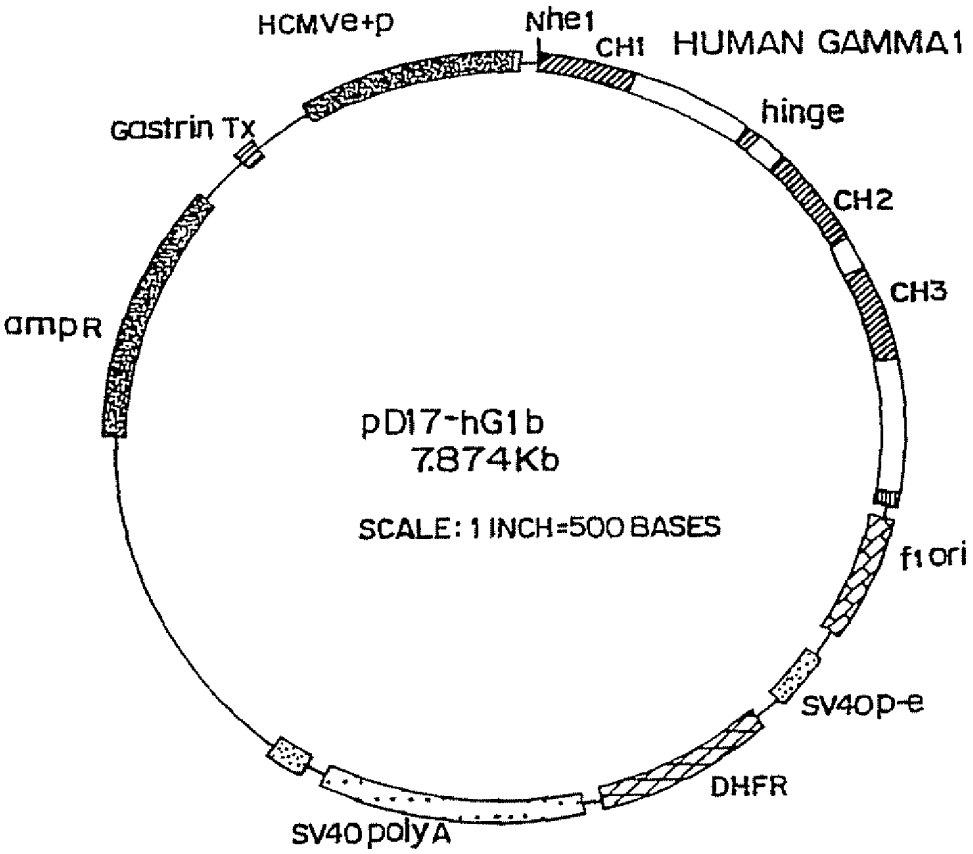

HCMVe+p
Nhe1
CH1
HUMAN GAMMA1
hinge
CH2
CH3
f1 ori
SV40p-e
DHFR
SV40 polyA
ampR
Gastrin Tx
pD17-hG1b
7.874Kb
SCALE: 1 INCH=500 BASES

FIG. 18A

(SEQ ID NO:22)

```
   1 GGTACCAATT  TAAATTGATA  TCTCCTTAGG  TCTCGAGTCT  CTAGATAACC
  51 GGTCAATCGA  TTGGAATTCT  TGCGGCCGCT  TGCTAGCCAC  CATGGAGTTG
 101 TGGTTAAGCT  TGGTCTTCCT  TGTCCTTGTT  TTAAAAGGTG  TCCAGTGTGA
 151 AGTGCAACTG  GTGGAGTCTG  GGGGAGGCTT  AGTGCAGCCT  GGAGGGTCCC
 201 TGCGACTTTC  CTGTGCTGCA  TCTGGATTCC  CGTTCAGTGA  CTATTACATG
 251 TATTGGGTTC  GCCAGGCTCC  AGGCAAGGGA  CTGGAGTGGG  TCTCATACAT
 301 TAGTCAAGAT  GGTGATATAA  CCGACTATGC  AGACTCCGTA  AAGGGTCGAT
 351 TCACCATCTC  CAGAGACAAT  GCAAAGAACA  GCCTGTACCT  GCAAATGAAC
 401 AGCCTGAGGG  ACGAGGACAC  AGCCGTGTAT  TACTGTGCAA  GAGGCCTGGC
 451 GGACGGGGCC  TGGTTTGCTT  ACTGGGGCCA  AGGGACTCTG  GTCACGGTCT
 501 CTTCCGCTAG  CACCAAGGGC  CCATCGGTCT  TCCCCCTGGC  ACCCTCCTCC
 551 AAGAGCACCT  CTGGGGGCAC  AGCGGCCCTG  GGCTGCCTGG  TCAAGGACTA
 601 CTTCCCCGAA  CCGGTGACGG  TGTCGTGGAA  CTCAGGCGCC  CTGACCAGCG
 651 GCGTGCACAC  CTTCCCGGCT  GTCCTACAGT  CCTCAGGACT  CTACTCCCTC
 701 AGCAGCGTGG  TCACCGTGCC  CTCCAGCAGC  TTGGGCACCC  AGACCTACAT
 751 CTGCAACGTG  AATCACAAGC  CCAGCAACAC  CAAGGTGGAC  AAGAAAGTTG
 801 GTGAGAGGCC  AGCACAGGGA  GGGAGGGTGT  CTGCTGGAAG  CCAGGCTCAG
 851 CGCTCCTGCC  TGGACGCATC  CCGGCTATGC  AGCCCCAGTC  CAGGGCAGCA
 901 AGGCAGGCCC  CGTCTGCCTC  TTCACCCGGA  GGCCTCTGCC  CGCCCCACTC
 951 ATGCTCAGGG  AGAGGGTCTT  CTGGCTTTTT  CCCCAGGCTC  TGGGCAGGCA
1001 CAGGCTAGGT  GCCCCTAACC  CAGGCCCTGC  ACACAAAGGG  GCAGGTGCTG
1051 GGCTCAGACC  TGCCAAGAGC  CATATCCGGG  AGGACCCTGC  CCCTGACCTA
1101 AGCCCACCCC  AAAGGCCAAA  CTCTCCACTC  CCTCAGCTCG  GACACCTTCT
1151 CTCCTCCCAG  ATTCCAGTAA  CTCCCAATCT  TCTCTCTGCA  GAGCCCAAAT
1201 CTTGTGACAA  AACTCACACA  TGCCCACCGT  GCCCAGGTAA  GCCAGCCCAG
1251 GCCTCGCCCT  CCAGCTCAAG  GCGGGACAGG  TGCCCTAGAG  TAGCCTGCAT
1301 CCAGGGACAG  GCCCCAGCCG  GGTGCTGACA  CGTCCACCTC  CATCTCTTCC
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FIG. 18B

(SEQ ID NO:22)

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                                235       237
1351 TCAGCACCTG AACTCCTGGG GGGACCGTCA GTCTTCCTCT TCCCCCCAAA
1401 ACCCAAGGAC ACCCTCATGA TCTCCCGGAC CCCTGAGGTC ACATGCGTGG
1451 TGGTGGACGT GAGCCACGAA GACCCTGAGG TCAAGTTCAA CTGGTACGTG
1501 GACGGCGTGG AGGTGCATAA TGCCAAGACA AAGCCGCGGG AGGAGCAGTA
1551 CAACAGCACG TACCGTGTGG TCAGCGTCCT CACCGTCCTG CACCAGGACT
                          318       320   322
1601 GGCTGAATGG CAAGGAGTAC AAGTGCAAGG TCTCCAACAA AGCCCTCCCA
                331
1651 GCCCCCATCG AGAAAACCAT CTCCAAAGCC AAAGGTGGGA CCCGTGGGGT
1701 GCGAGGGCCA CATGGACAGA GGCCGGCTCG GCCCACCCTC TGCCCTGAGA
1751 GTGACCGCTG TACCAACCTC TGTCCCTACA GGGCAGCCCC GAGAACCACA
1801 GGTGTACACC CTGCCCCCAT CCCGGGATGA GCTGACCAAG AACCAGGTCA
1851 GCCTGACCTG CCTGGTCAAA GGCTTCTATC CCAGCGACAT CGCCGTGGAG
1901 TGGGAGAGCA ATGGGCAGCC GGAGAACAAC TACAAGACCA CGCCTCCCGT
1951 GCTGGACTCC GACGGCTCCT TCTTCCTCTA CAGCAAGCTC ACCGTGGACA
2001 AGAGCAGGTG GCAGCAGGGG AACGTCTTCT CATGCTCCGT GATGCATGAG
2051 GCTCTGCACA ACCACTACAC GCAGAAGAGC CTCTCCCTGT CTCCGGGTAA
2101 ATGAGTGCGA CGGCCGGCAA GCCCCCGCTC CCCGGGCTCT CGCGGTCGCA
2151 CGAGGATGCT TGGCACGTAC CCCCTGTACA TACTTCCCGG GCGCCCAGCA
2201 TGGAAATAAA GCACCCAGCG CTGCCCTGGG CCCCTGCGAG ACTGTGATGG
2251 TTCTTTCCAC GGGTCAGGCC GAGTCTGAGG CCTGAGTGGC ATGAGGGAGG
2301 CAGAGCGGGT CCCACTGTCC CCACACTGGC CCAGGCTGTG CAGGTGTGCC
2351 TGGGCCCCCT AGGGTGGGGC TCAGCCAGGG GCTGCCCTCG GCAGGGTGGG
2401 GGATTTGCCA GCGTGGCCCT CCCTCCAGCA GCACCTGCCC TGGGCTGGGC
2451 CACGGGAAGC CCTAGGAGCC CCTGGGGACA GACACACAGC CCCTGCCTCT
2501 GTAGGAGACT GTCCTGTTCT GTGAGCGCCC CTGTCCTCCC GACCTCCATG
2551 CCCACTCGGG GGCATGCCTA GTCCATGTGC GTAGGGACAG GCCCTCCCTC
2601 ACCCATCTAC CCCCACGGCA CTAACCCCTG GCTGCCCTGC CCAGCCTCGC
2651 ACCCGCATGG GGACACAACC GACTCCGGGG ACATGCACTC TCGGGCCCTG
2701 TGGAGGGACT GGTGCAGATG CCCACACACA CACTCAGCCC AGACCCGTTC
2751 AACAAACCCC GCACTGAGGT TGGCCGGCCA CACGGCCACC ACACACACAC
2801 GTGCACGCCT CACACACGGA GCCTCACCCG GGCGAACTGC ACAGCACCCA
```

FIG. 18C

(SEQ ID NO:22)

```
2851 GACCAGAGCA  AGGTCCTCGC  ACACGTGAAC  ACTCCTCGGA  CACAGGCCCC
2901 CACGAGCCCC  ACGCGGCACC  TCAAGGCCCA  CGAGCCTCTC  GGCAGCTTCT
2951 CCACATGCTG  ACCTGCTCAG  ACAAACCCAG  CCCTCCTCTC  ACAAGGGTGC
3001 CCCTGCAGCC  GCCACACACA  CACAGGGGAT  CACACACCAC  GTCACGTCCC
3051 TGGCCCTGGC  CCACTTCCCA  GTGCCGCCCT  TCCCTGCAGG  ACGGATCAGC
3101 CTCGACTGTG  CCTTCTAGTT  GCCAGCCATC  TGTTGTTTGC  CCCTCCCCCG
3151 TGCCTTCCTT  GACCCTGGAA  GGTGCCACTC  CCACTGTCCT  TTCCTAATAA
3201 AATGAGGAAA  TTGCATCGCA  TTGTCTGAGT  AGGTGTCATT  CTATTCTGGG
3251 GGGTGGGGTG  GGGCAGGACA  GCAAGGGGGA  GGATTGGGAA  GACAATAGCA
3301 GGCATGCTGG  GGATGCGGTG  GGCTCTATGG  CTTCTGAGGC  GGAAAGAACC
3351 AGCTGGGGCT  CTAGGGGGTA  TCCCCACGCG  CCCTGTAGCG  GCGCATTAAG
3401 CGCGGCGGGT  GTGGTGGTTA  CGCGCAGCGT  GACCGCTACA  CTTGCCAGCG
3451 CCCTAGCGCC  CGCTCCTTTC  GCTTTCTTCC  CTTCCTTTCT  CGCCACGTTC
3501 GCCGGGCCTC  TCAAAAAAGG  GAAAAAAAGC  ATGCATCTCA  ATTAGTCAGC
3551 AACCATAGTC  CCGCCCCTAA  CTCCGCCCAT  CCCGCCCCTA  ACTCCGCCCA
3601 GTTCCGCCCA  TTCTCCGCCC  CATGGCTGAC  TAATTTTTTT  TATTTATGCA
3651 GAGGCCGAGG  CCGCCTCGGC  CTCTGAGCTA  TTCCAGAAGT  AGTGAGGAGG
3701 CTTTTTTGGA  GGCCTAGGCT  TTTGCAAAAA  GCTTGGACAG  CTCAGGGCTG
3751 CGATTTCGCG  CCAAACTTGA  CGGCAATCCT  AGCGTGAAGG  CTGGTAGGAT
3801 TTTATCCCCG  CTGCCATCAT  GGTTCGACCA  TTGAACTGCA  TCGTCGCCGT
3851 GTCCCAAAAT  ATGGGGATTG  GCAAGAACGG  AGACCTACCC  TGGCCTCCGC
3901 TCAGGAACGA  GTTCAAGTAC  TTCCAAAGAA  TGACCACAAC  CTCTTCAGTG
3951 GAAGGTAAAC  AGAATCTGGT  GATTATGGGT  AGGAAAACCT  GGTTCTCCAT
4001 TCCTGAGAAG  AATCGACCTT  TAAAGGACAG  AATTAATATA  GTTCTCAGTA
4051 GAGAACTCAA  AGAACCACCA  CGAGGAGCTC  ATTTTCTTGC  CAAAAGTTTG
4101 GATGATGCCT  TAAGACTTAT  TGAACAACCG  GAATTGGCAA  GTAAAGTAGA
4151 CATGGTTTGG  ATAGTCGGAG  GCAGTTCTGT  TTACCAGGAA  GCCATGAATC
4201 AACCAGGCCA  CCTTAGACTC  TTTGTGACAA  GGATCATGCA  GGAATTTGAA
4251 AGTGACACGT  TTTTCCCAGA  AATTGATTTG  GGGAAATATA  AACTTCTCCC
4301 AGAATACCCA  GGCGTCCTCT  CTGAGGTCCA  GGAGGAAAAA  GGCATCAAGT
```

FIG. 18D

(SEQ ID NO:22)

4351	ATAAGTTTGA	AGTCTACGAG	AAGAAAGACT	AACAGGAAGA	TGCTTTCAAG
4401	TTCTCTGCTC	CCCTCCTAAA	GCTATGCATT	TTTATAAGAC	CATGGGACTT
4451	TTGCTGGCTT	TAGATCTCTT	TGTGAAGGAA	CCTTACTTCT	GTGGTGTGAC
4501	ATAATTGGAC	AAACTACCTA	CAGAGATTTA	AAGCTCTAAG	GTAAATATAA
4551	AATTTTTAAG	TGTATAATGT	GTTAAACTAC	TGATTCTAAT	TGTTTGTGTA
4601	TTTTAGATTC	CAACCTATGG	AACTGATGAA	TGGGAGCAGT	GGTGGAATGC
4651	CTTTAATGAG	GAAAACCTGT	TTTGCTCAGA	AGAAATGCCA	TCTAGTGATG
4701	ATGAGGCTAC	TGCTGACTCT	CAACATTCTA	CTCCTCCAAA	AAAGAAGAGA
4751	AAGGTAGAAG	ACCCCAAGGA	CTTTCCTTCA	GAATTGCTAA	GTTTTTTGAG
4801	TCATGCTGTG	TTTAGTAATA	GAACTCTTGC	TTGCTTTGCT	ATTTACACCA
4851	CAAAGGAAAA	AGCTGCACTG	CTATACAAGA	AAATTATGGA	AAAATATTCT
4901	GTAACCTTTA	TAAGTAGGCA	TAACAGTTAT	AATCATAACA	TACTGTTTTT
4951	TCTTACTCCA	CACAGGCATA	GAGTGTCTGC	TATTAATAAC	TATGCTCAAA
5001	AATTGTGTAC	CTTTAGCTTT	TTAATTTGTA	AAGGGGTTAA	TAAGGAATAT
5051	TTGATGTATA	GTGCCTTGAC	TAGAGATCAT	AATCAGCCAT	ACCACATTTG
5101	TAGAGGTTTT	ACTTGCTTTA	AAAAACCTCC	CACACCTCCC	CCTGAACCTG
5151	AAACATAAAA	TGAATGCAAT	TGTTGTTGTT	AACTTGTTTA	TTGCAGCTTA
5201	TAATGGTTAC	AAATAAAGCA	ATAGCATCAC	AAATTTCACA	AATAAAGCAT
5251	TTTTTTCACT	GCATTCTAGT	TGTGGTTTGT	CCAAACTCAT	CAATGTATCT
5301	TATCATGTCT	GGATCGGCTG	GATGATCCTC	CAGCGCGGGG	ATCTCATGCT
5351	GGAGTTCTTC	GCCCACCCCA	ACTTGTTTAT	TGCAGCTTAT	AATGGTTACA
5401	AATAAAGCAA	TAGCATCACA	AATTTCACAA	ATAAAGCATT	TTTTTCACTG
5451	CATTCTAGTT	GTGGTTTGTC	CAAACTCATC	AATGTATCTT	ATCATGTCTG
5501	TATACCGTCG	ACCTCTAGCT	AGAGCTTGGC	GTAATCATGG	TCATAGCTGT
5551	TTCCTGTGTG	AAATTGTTAT	CCGCTCACAA	TTCCACACAA	CATACGAGCC
5601	GGAAGCATAA	AGTGTAAAGC	CTGGGGTGCC	TAATGAGTGA	GCTAACTCAC
5651	ATTAATTGCG	TTGCGCTCAC	TGCCCGCTTT	CCAGTCGGGA	AACCTGTCGT
5701	GCCAGCTGCA	TTAATGAATC	GGCCAACGCG	CGGGGAGAGG	CGGTTTGCGT
5751	ATTGGGCGCT	CTTCCGCTTC	CTCGCTCACT	GACTCGCTGC	GCTCGGTCGT
5801	TCGGCTGCGG	CGAGCGGTAT	CAGCTCACTC	AAAGGCGGTA	ATACGGTTAT

FIG. 18E

(SEQ ID NO:22)

5851	CCACAGAATC	AGGGGATAAC	GCAGGAAAGA	ACATGTGAGC	AAAAGGCCAG
5901	CAAAAGGCCA	GGAACCGTAA	AAAGGCCGCG	TTGCTGGCGT	TTTTCCATAG
5951	GCTCCGCCCC	CCTGACGAGC	ATCACAAAAA	TCGACGCTCA	AGTCAGAGGT
6001	GGCGAAACCC	GACAGGACTA	TAAAGATACC	AGGCGTTTCC	CCCTGGAAGC
6051	TCCCTCGTGC	GCTCTCCTGT	TCCGACCCTG	CCGCTTACCG	GATACCTGTC
6101	CGCCTTTCTC	CCTTCGGGAA	GCGTGGCGCT	TTCTCAATGC	TCACGCTGTA
6151	GGTATCTCAG	TTCGGTGTAG	GTCGTTCGCT	CCAAGCTGGG	CTGTGTGCAC
6201	GAACCCCCCG	TTCAGCCCGA	CCGCTGCGCC	TTATCCGGTA	ACTATCGTCT
6251	TGAGTCCAAC	CCGGTAAGAC	ACGACTTATC	GCCACTGGCA	GCAGCCACTG
6301	GTAACAGGAT	TAGCAGAGCG	AGGTATGTAG	GCGGTGCTAC	AGAGTTCTTG
6351	AAGTGGTGGC	CTAACTACGG	CTACACTAGA	AGGACAGTAT	TTGGTATCTG
6401	CGCTCTGCTG	AAGCCAGTTA	CCTTCGGAAA	AAGAGTTGGT	AGCTCTTGAT
6451	CCGGCAAACA	AACCACCGCT	GGTAGCGGTG	GTTTTTTTGT	TTGCAAGCAG
6501	CAGATTACGC	GCAGAAAAAA	AGGATCTCAA	GAAGATCCTT	TGATCTTTTC
6551	TACGGGGTCT	GACGCTCAGT	GGAACGAAAA	CTCACGTTAA	GGGATTTTGG
6601	TCATGAGATT	ATCAAAAAGG	ATCTTCACCT	AGATCCTTTT	AAATTAAAAA
6651	TGAAGTTTTA	AATCAATCTA	AAGTATATAT	GAGTAAACTT	GGTCTGACAG
6701	TTACCAATGC	TTAATCAGTG	AGGCACCTAT	CTCAGCGATC	TGTCTATTTC
6751	GTTCATCCAT	AGTTGCCTGA	CTCCCCGTCG	TGTAGATAAC	TACGATACGG
6801	GAGGGCTTAC	CATCTGGCCC	CAGTGCTGCA	ATGATACCGC	GAGACCCACG
6851	CTCACCGGCT	CCAGATTTAT	CAGCAATAAA	CCAGCCAGCC	GGAAGGGCCG
6901	AGCGCAGAAG	TGGTCCTGCA	ACTTTATCCG	CCTCCATCCA	GTCTATTAAT
6951	TGTTGCCGGG	AAGCTAGAGT	AAGTAGTTCG	CCAGTTAATA	GTTTGCGCAA
7001	CGTTGTTGCC	ATTGCTACAG	GCATCGTGGT	GTCACGCTCG	TCGTTTGGTA
7051	TGGCTTCATT	CAGCTCCGGT	TCCCAACGAT	CAAGGCGAGT	TACATGATCC
7101	CCCATGTTGT	GCAAAAAAGC	GGTTAGCTCC	TTCGGTCCTC	CGATCGTTGT
7151	CAGAAGTAAG	TTGGCCGCAG	TGTTATCACT	CATGGTTATG	GCAGCACTGC
7201	ATAATTCTCT	TACTGTCATG	CCATCCGTAA	GATGCTTTTC	TGTGACTGGT
7251	GAGTACTCAA	CCAAGTCATT	CTGAGAATAG	TGTATGCGGC	GACCGAGTTG
7301	CTCTTGCCCG	GCGTCAATAC	GGGATAATAC	CGCGCCACAT	AGCAGAACTT

FIG. 18F

(SEQ ID NO:22)

7351	TAAAAGTGCT	CATCATTGGA	AAACGTTCTT	CGGGGCGAAA	ACTCTCAAGG
7401	ATCTTACCGC	TGTTGAGATC	CAGTTCGATG	TAACCCACTC	GTGCACCCAA
7451	CTGATCTTCA	GCATCTTTTA	CTTTCACCAG	CGTTTCTGGG	TGAGCAAAAA
7501	CAGGAAGGCA	AAATGCCGCA	AAAAAGGGAA	TAAGGGCGAC	ACGGAAATGT
7551	TGAATACTCA	TACTCTTCCT	TTTTCAATAT	TATTGAAGCA	TTTATCAGGG
7601	TTATTGTCTC	ATGAGCGGAT	ACATATTTGA	ATGTATTTAG	AAAAATAAAC
7651	AAATAGGGGT	TCCGCGCACA	TTTCCCCGAA	AAGTGCCACC	TGACGTCGAC
7701	GGATCGGGAG	ATCTGCTAGG	TGACCTGAGG	CGCGCCGGCT	TCGAATAGCC
7751	AGAGTAACCT	TTTTTTTTAA	TTTTATTTTA	TTTTATTTTT	GAGATGGAGT
7801	TTGGCGCCGA	TCTCCCGATC	CCCTATGGTC	GACTCTCAGT	ACAATCTGCT
7851	CTGATGCCGC	ATAGTTAAGC	CAGTATCTGC	TCCCTGCTTG	TGTGTTGGAG
7901	GTCGCTGAGT	AGTGCGCGAG	CAAAATTTAA	GCTACAACAA	GGCAAGGCTT
7951	GACCGACAAT	TGCATGAAGA	ATCTGCTTAG	GGTTAGGCGT	TTTGCGCTGC
8001	TTCGCGATGT	ACGGGCCAGA	TATACGCGTT	GACATTGATT	ATTGACTAGT
8051	TATTAATAGT	AATCAATTAC	GGGGTCATTA	GTTCATAGCC	CATATATGGA
8101	GTTCCGCGTT	ACATAACTTA	CGGTAAATGG	CCCGCCTGGC	TGACCGCCCA
8151	ACGACCCCCG	CCCATTGACG	TCAATAATGA	CGTATGTTCC	CATAGTAACG
8201	CCAATAGGGA	CTTTCCATTG	ACGTCAATGG	GTGGACTATT	TACGGTAAAC
8251	TGCCCACTTG	GCAGTACATC	AAGTGTATCA	TATGCCAAGT	ACGCCCCCTA
8301	TTGACGTCAA	TGACGGTAAA	TGGCCCGCCT	GGCATTATGC	CCAGTACATG
8351	ACCTTATGGG	ACTTTCCTAC	TTGGCAGTAC	ATCTACGTAT	TAGTCATCGC
8401	TATTACCATG	GTGATGCGGT	TTTGGCAGTA	CATCAATGGG	CGTGGATAGC
8451	GGTTTGACTC	ACGGGGATTT	CCAAGTCTCC	ACCCCATTGA	CGTCAATGGG
8501	AGTTTGTTTT	GGCACCAAAA	TCAACGGGAC	TTTCCAAAAT	GTCGTAACAA
8551	CTCCGCCCCA	TTGACGCAAA	TGGGCGGTAG	GCGTGTACGG	TGGGAGGTCT
8601	ATATAAGCAG	AGCTCTCTGG	CTAACTAGAG	AACCCACTGC	TTACTGGCTT
8651	ATCGAAATTA	ATACGACTCA	CTATAGGGAG	ACCCAAGCTT	

FIG. 19A
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

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                10                  20                  30                  40                  50                  60
GGTACCAATT  TAAATTGATA  TCTCCTTAGG  TCTCGAGTCT  CTAGATAACC  GGTCAATCGA
CCATGGTTAA  ATTTAACTAT  AGAGGAATCC  AGAGCTCAGA  GATCTATTGG  CCAGTTAGCT

                70                  80                  90                 100                 110                 120
TTGGAATTCT  TGCGGCCGCT  TGCTAGCACC  AAGGGCCCAT  CGGTCTTCCC  CCTGGCACCC
AACCTTAAGA  ACGCCGGCGA  ACGATCGTGG  TTCCCGGGTA  GCCAGAAGGG  GGACCGTGGG

                130                 140                 150                 160                 170                 180
TCCTCCAAGA  GCACCTCTGG  GGGCACAGCG  GCCCTGGGCT  GCCTGGTCAA  GGACTACTTC
AGGAGGTTCT  CGTGGAGACC  CCCGTGTCGC  CGGGACCCGA  CGGACCAGTT  CCTGATGAAG

                190                 200                 210                 220                 230                 240
CCCGAACCGG  TGACGGTGTC  GTGGAACTCA  GGCGCCCTGA  CCAGCGGCGT  GCACACCTTC
GGGCTTGGCC  ACTGCCACAG  CACCTTGAGT  CCGCGGGACT  GGTCGCCGCA  CGTGTGGAAG

                250                 260                 270                 280                 290                 300
CCGGCTGTCC  TACAGTCCTC  AGGACTCTAC  TCCCTCAGCA  GCGTGGTCAC  CGTGCCCTCC
GGCCGACAGG  ATGTCAGGAG  TCCTGAGATG  AGGGAGTCGT  CGCACCAGTG  GCACGGGAGG

                310                 320                 330                 340                 350                 360
AGCAGCTTGG  GCACCCAGAC  CTACATCTGC  AACGTGAATC  ACAAGCCCAG  CAACACCAAG
TCGTCGAACC  CGTGGGTCTG  GATGTAGACG  TTGCACTTAG  TGTTCGGGTC  GTTGTGGTTC

                370                 380                 390                 400                 410                 420
GTGGACAAGA  AAGTTGGTGA  GAGGCCAGCA  CAGGGAGGGA  GGGTGTCTGC  TGGAAGCCAG
CACCTGTTCT  TTCAACCACT  CTCCGGTCGT  GTCCCTCCCT  CCCACAGACG  ACCTTCGGTC

                430                 440                 450                 460                 470                 480
GCTCAGCGCT  CCTGCCTGGA  CGCATCCCGG  CTATGCAGCC  CCAGTCCAGG  GCAGCAAGGC
CGAGTCGCGA  GGACGGACCT  GCGTAGGGCC  GATACGTCGG  GGTCAGGTCC  CGTCGTTCCG

                490                 500                 510                 520                 530                 540
AGGCCCCGTC  TGCCTCTTCA  CCCGGAGGCC  TCTGCCCGCC  CCACTCATGC  TCAGGGAGAG
TCCGGGGCAG  ACGGAGAAGT  GGGCCTCCGG  AGACGGGCGG  GGTGAGTACG  AGTCCCTCTC

                550                 560                 570                 580                 590                 600
GGTCTTCTGG  CTTTTTCCCC  AGGCTCTGGG  CAGGCACAGG  CTAGGTGCCC  CTAACCCAGG
CCAGAAGACC  GAAAAAGGGG  TCCGAGACCC  GTCCGTGTCC  GATCCACGGG  GATTGGGTCC
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FIG. 19B
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

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FIG. 19C
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

FIG. 19D
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

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1810                1820                1830                1840                1850                1860
CCTGGGCCCC          TGCGAGACTG          TGATGGTTCT          TTCCACGGGT          CAGGCCGAGT          CTGAGGCCTG
GGACCCGGGG          ACGCTCTGAC          ACTACCAAGA          AAGGTGCCCA          GTCCGGCTCA          GACTCCGGAC

1870                1880                1890                1900                1910                1920
AGTGGCATGA          GGGAGGCAGA          GCGGGTCCCA          CTGTCCCCAC          ACTGGCCCAG          GCTGTGCAGG
TCACCGTACT          CCCTCCGTCT          CGCCCAGGGT          GACAGGGGTG          TGACCGGGTC          CGACACGTCC

1930                1940                1950                1960                1970                1980
TGTGCCTGGG          CCCCCTAGGG          TGGGGCTCAG          CCAGGGGCTG          CCCTCGGCAG          GGTGGGGGAT
ACACGGACCC          GGGGGATCCC          ACCCCGAGTC          GGTCCCCGAC          GGGAGCCGTC          CCACCCCCTA

1990                2000                2010                2020                2030                2040
TTGCCAGCGT          GGCCCTCCCT          CCAGCAGCAC          CTGCCCTGGG          CTGGGCCACG          GGAAGCCCTA
AACGGTCGCA          CCGGGAGGGA          GGTCGTCGTG          GACGGGACCC          GACCCGGTGC          CCTTCGGGAT

2050                2060                2070                2080                2090                2100
GGAGCCCCTG          GGGACAGACA          CACAGCCCCT          GCCTCTGTAG          GAGACTGTCC          TGTTCTGTGA
CCTCGGGGAC          CCCTGTCTGT          GTGTCGGGGA          CGGAGACATC          CTCTGACAGG          ACAAGACACT

2110                2120                2130                2140                2150                2160
GCGCCCCTGT          CCTCCCCGACC         TCCATGCCCA          CTCGGGGGCA          TGCTGGGGAT          GCGGTGGGCT
CGCGGGGACA          GGAGGGCTGG          AGGTACGGGT          GAGCCCCCGT          ACGACCCCTA          CGCCACCCGA

2170                2180                2190                2200                2210                2220
CTATGGCTTC          TGAGGCGGAA          AGAACCAGCT          GGGGCTCTAG          GGGGTATCCC          CACGCGCCCT
GATACCGAAG          ACTCCGCCTT          TCTTGGTCGA          CCCCGAGATC          CCCCATAGGG          GTGCGCGGGA

2230                2240                2250                2260                2270                2280
GTAGCGGCGC          ATTAAGCGCG          GCGGGTGTGG          TGGTTACGCG          CAGCGTGACC          GCTACACTTG
CATCGCCGCG          TAATTCGCGC          CGCCCACACC          ACCAATGCGC          GTCGCACTGG          CGATGTGAAC

2290                2300                2310                2320                2330                2340
CCAGCGCCCT          AGCGCCCGCT          CCTTTCGCTT          TCTTCCCTTC          CTTTCTCGCC          ACGTTCGCCG
GGTCGCGGGA          TCGCGGGCGA          GGAAAGCGAA          AGAAGGGAAG          GAAAGAGCGG          TGCAAGCGGC

2350                2360                2370                2380                2390                2400
GCTTTCCCCG          TCAAGCTCTA          AATCGGGGCA          TCCCTTTAGG          GTTCCGATTT          AGTGCTTTAC
CGAAAGGGGC          AGTTCGAGAT          TTAGCCCCGT          AGGGAAATCC          CAAGGCTAAA          TCACGAAATG
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FIG. 19E
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

FIG. 19F
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

```
                3010       3020       3030       3040       3050       3060
TCATGGTTCG ACCATTGAAC TGCATCGTCG CCGTGTCCCA AAATATGGGG ATTGGCAAGA
AGTACCAAGC TGGTAACTTG ACGTAGCAGC GGCACAGGGT TTTATACCCC TAACCGTTCT

                3070       3080       3090       3100       3110       3120
ACGGAGACCT ACCCTGGCCT CCGCTCAGGA ACGAGTTCAA GTACTTCCAA AGAATGACCA
TGCCTCTGGA TGGGACCGGA GGCGAGTCCT TGCTCAAGTT CATGAAGGTT TCTTACTGGT

                3130       3140       3150       3160       3170       3180
CAACCTCTTC AGTGGAAGGT AAACAGAATC TGGTGATTAT GGGTAGGAAA ACCTGGTTCT
GTTGGAGAAG TCACCTTCCA TTTGTCTTAG ACCACTAATA CCCATCCTTT TGGACCAAGA

                3190       3200       3210       3220       3230       3240
CCATTCCTGA GAAGAATCGA CCTTTAAAGG ACAGAATTAA TATAGTTCTC AGTAGAGAAC
GGTAAGGACT CTTCTTAGCT GGAAATTTCC TGTCTTAATT ATATCAAGAG TCATCTCTTG

                3250       3260       3270       3280       3290       3300
TCAAAGAACC ACCACGAGGA GCTCATTTTC TTGCCAAAAG TTTGGATGAT GCCTTAAGAC
AGTTTCTTGG TGGTGCTCCT CGAGTAAAAG AACGGTTTTC AAACCTACTA CGGAATTCTG

                3310       3320       3330       3340       3350       3360
TTATTGAACA ACCGGAATTG GCAAGTAAAG TAGACATGGT TTGGATAGTC GGAGGCAGTT
AATAACTTGT TGGCCTTAAC CGTTCATTTC ATCTGTACCA AACCTATCAG CCTCCGTCAA

                3370       3380       3390       3400       3410       3420
CTGTTTACCA GGAAGCCATG AATCAACCAG GCCACCTTAG ACTCTTTGTG ACAAGGATCA
GACAAATGGT CCTTCGGTAC TTAGTTGGTC CGGTGGAATC TGAGAACAC TGTTCCTAGT

                3430       3440       3450       3460       3470       3480
TGCAGGAATT TGAAAGTGAC ACGTTTTTCC CAGAAATTGA TTTGGGGAAA TATAACTTC
ACGTCCTTAA ACTTTCACTG TGCAAAAAGG GTCTTTAACT AAACCCCTTT ATATTTGAAG

                3490       3500       3510       3520       3530       3540
TCCCAGAATA CCCAGGCGTC CTCTCTGAGG TCCAGGAGGA AAAAGGCATC AAGTATAAGT
AGGGTCTTAT GGGTCCGCAG GAGAGACTCC AGGTCCTCCT TTTTCCGTAG TTCATATTCA

                3550       3560       3570       3580       3590       3600
TTGAAGTCTA CGAGAAGAAA GACTAACAGG AAGATGCTTT CAAGTTCTCT GCTCCCCTCC
AACTTCAGAT GCTCTTCTTT CTGATTGTCC TTCTACGAAA GTTCAAGAGA CGAGGGGAGG
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FIG. 19G
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

FIG. 19H
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

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FIG. 19I
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

FIG. 19J
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

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                5410        5420        5430        5440        5450        5460
CCGACCGCTG  CGCCTTATCC  GGTAACTATC  GTCTTGAGTC  CAACCCGGTA  AGACACGACT
GGCTGGCGAC  GCGGAATAGG  CCATTGATAG  CAGAACTCAG  GTTGGGCCAT  TCTGTGCTGA

                5470        5480        5490        5500        5510        5520
TATCGCCACT  GGCAGCAGCC  ACTGGTAACA  GGATTAGCAG  AGCGAGGTAT  GTAGGCGGTG
ATAGCGGTGA  CCGTCGTCGG  TGACCATTGT  CCTAATCGTC  TCGCTCCATA  CATCCGCCAC

                5530        5540        5550        5560        5570        5580
CTACAGAGTT  CTTGAAGTGG  TGGCCTAACT  ACGGCTACAC  TAGAAGGACA  GTATTTGGTA
GATGTCTCAA  GAACTTCACC  ACCGGATTGA  TGCCGATGTG  ATCTTCCTGT  CATAAACCAT

                5590        5600        5610        5620        5630        5640
TCTGCGCTCT  GCTGAAGCCA  GTTACCTTCG  GAAAAGAGTT  TGGTAGCTCT  TGATCCGGCA
AGACGCGAGA  CGACTTCGGT  CAATGGAAGC  CTTTTTCTCA  ACCATCGAGA  ACTAGGCCGT

                5650        5660        5670        5680        5690        5700
AACAAACCAC  CGCTGGTAGC  GGTGGTTTTT  TTGTTTGCAA  GCAGCAGATT  ACGCGCAGAA
TTGTTTGGTG  GCGACCATCG  CCACCAAAAA  AACAAACGTT  CGTCGTCTAA  TGCGCGTCTT

                5710        5720        5730        5740        5750        5760
AAAAAGGATC  TCAAGAAGAT  CCTTTGATCT  TTTCTACGGG  GTCTGACGCT  CAGTGGAACG
TTTTTCCTAG  AGTTCTTCTA  GGAAACTAGA  AAAGATGCCC  CAGACTGCGA  GTCACCTTGC

                5770        5780        5790        5800        5810        5820
AAAACTCACG  TTAAGGGATT  TTGGTCATGA  GATTATCAAA  AAGGATCTTC  ACCTAGATCC
TTTTGAGTGC  AATTCCCTAA  AACCAGTACT  CTAATAGTTT  TTCCTAGAAG  TGGATCTAGG

                5830        5840        5850        5860        5870        5880
TTTTAAATTA  AAAATGAAGT  TTTAAATCAA  TCTAAAGTAT  ATATGAGTAA  ACTTGGTCTG
AAAATTTAAT  TTTTACTTCA  AAATTTAGTT  AGATTTCATA  TATACTCATT  TGAACCAGAC

                5890        5900        5910        5920        5930        5940
ACAGTTACCA  ATGCTTAATC  AGTGAGGCAC  CTATCTCAGC  GATCTGTCTA  TTTCGTTCAT
TGTCAATGGT  TACGAATTAG  TCACTCCGTG  GATAGAGTCG  CTAGACAGAT  AAAGCAAGTA

                5950        5960        5970        5980        5990        6000
CCATAGTTGC  CTGACTCCCC  GTCGTGTAGA  TAACTACGAT  ACGGGAGGGC  TTACCATCTG
GGTATCAACG  GACTGAGGGG  CAGCACATCT  ATTGATGCTA  TGCCCTCCCG  AATGGTAGAC
```

FIG. 19K
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

```
                                                
```

FIG. 19L
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

pD17-hG1b

6610 6620 6630 6640 6650 6660
GATCCAGTTC GATGTAACCC ACTCGTGCAC CCAACTGATC TTCAGCATCT TTTACTTTCA
CTAGGTCAAG CTACATTGGG TGAGCACGTG GGTTGACTAG AAGTCGTAGA AAATGAAAGT

6670 6680 6690 6700 6710 6720
CCAGCGTTTC TGGGTGAGCA AAAACAGGAA GGCAAAATGC CGCAAAAAAG GGAATAAGGG
GGTCGCAAAG ACCCACTCGT TTTTGTCCTT CCGTTTTACG GCGTTTTTTC CCTTATTCCC

6730 6740 6750 6760 6770 6780
CGACACGGAA ATGTTGAATA CTCATACTCT TCCTTTTTCA ATATTATTGA AGCATTTATC
GCTGTGCCTT TACAACTTAT GAGTATGAGA AGGAAAAAGT TATAATAACT TCGTAAATAG

6790 6800 6810 6820 6830 6840
AGGGTTATTG TCTCATGAGC GGATACATAT TTGAATGTAT TTAGAAAAAT AAACAAATAG
TCCCAATAAC AGAGTACTCG CCTATGTATA AACTTACATA AATCTTTTTA TTTGTTTATC

6850 6860 6870 6880 6890 6900
GGGTTCCGCG CACATTTCCC CGAAAAGTGC CACCTGACGT CGACGGATCG GGAGATCTGC
CCCAAGGCGC GTGTAAAGGG GCTTTTCACG GTGGACTGCA GCTGCCTAGC CCTCTAGACG

6910 6920 6930 6940 6950 6960
TAGGTGACCT GAGGCGCGCC GGCTTCGAAT AGCCAGAGTA ACCTTTTTTT TTAATTTTAT
ATCCACTGGA CTCCGCGCGG CCGAAGCTTA TCGGTCTCAT TGGAAAAAAA AATTAAAATA

6970 6980 6990 7000 7010 7020
TTTATTTTAT TTTTGAGATG GAGTTTGGCG CCGATCTCCC GATCCCCTAT GGTCGACTCT
AAATAAAATA AAAACTCTAC CTCAAACCGC GGCTAGAGGG CTAGGGGATA CCAGCTGAGA

7030 7040 7050 7060 7070 7080
CAGTACAATC TGCTCTGATG CCGCATAGTT AAGCCAGTAT CTGCTCCCTG CTTGTGTGTT
GTCATGTTAG ACGAGACTAC GGCGTATCAA TTCGGTCATA GACGAGGGAC GAACACACAA

7090 7100 7110 7120 7130 7140
GGAGGTCGCT GAGTAGTGCG CGAGCAAAAT TTAAGCTACA ACAAGGCAAG GCTTGACCGA
CCTCCAGCGA CTCATCACGC GCTCGTTTTA AATTCGATGT TGTTCCGTTC CGAACTGGCT

7150 7160 7170 7180 7190 7200
CAATTGCATG AAGAATCTGC TTAGGGTTAG GCGTTTTGCG CTGCTTCGCG ATGTACGGGC
GTTAACGTAC TTCTTAGACG AATCCCAATC CGCAAAACGC GACGAAGCGC TACATGCCCG

FIG. 19M
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

FIG. 19N
Primary Sequence = SEQ ID NO:23
Complementary Sequence = SEQ ID NO:29

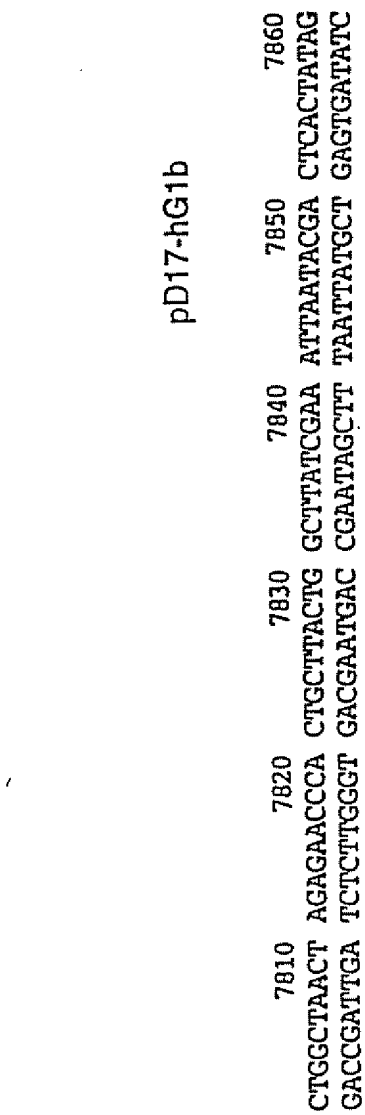

FIG. 20

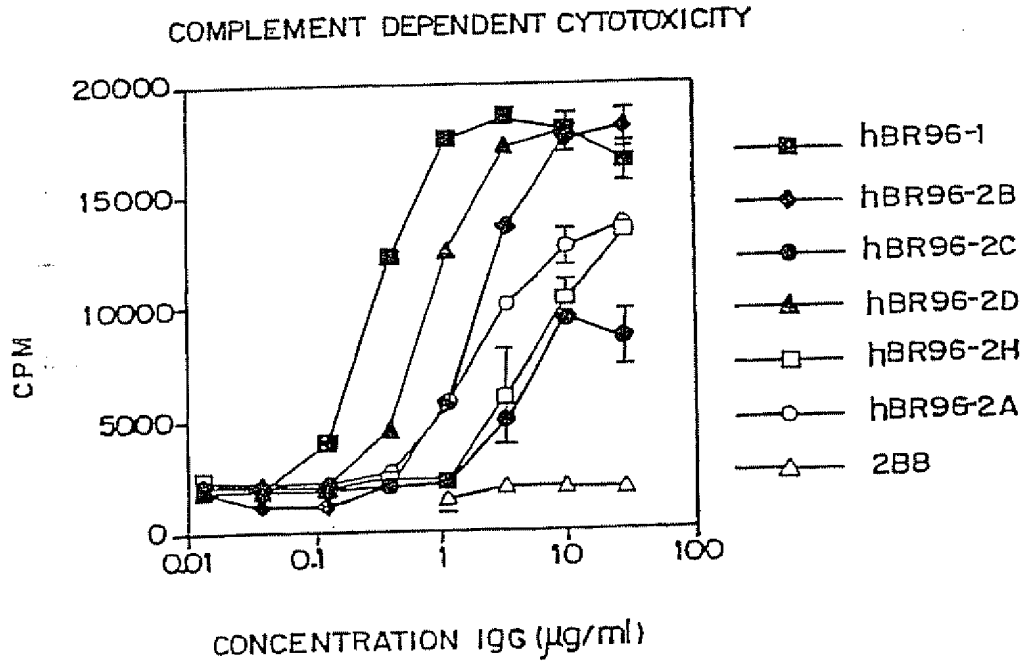
COMPLEMENT DEPENDENT CYTOTOXICITY
CPM
20000
15000
10000
5000
0
0.01
0.1
1
10
100
CONCENTRATION IgG (µg/ml)
hBR96-1
hBR96-2B
hBR96-2C
hBR96-2D
hBR96-2H
hBR96-2A
2B8

FIG. 21

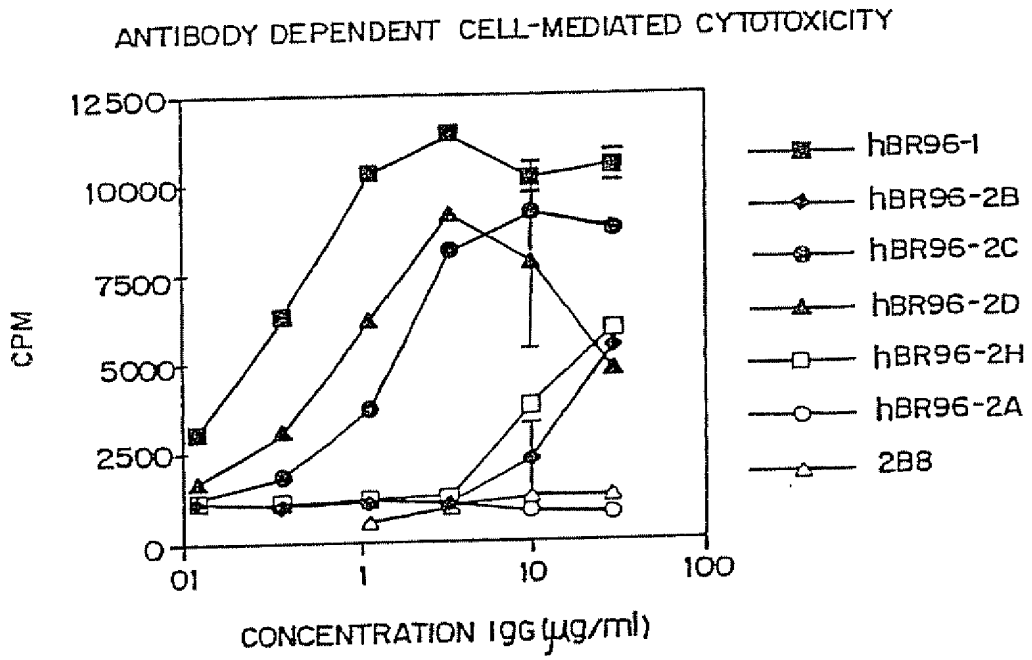
ANTIBODY DEPENDENT CELL-MEDIATED CYTOTOXICITY
12500
10000
7500
5000
2500
0
CPM
01
1
10
100
CONCENTRATION IgG (µg/ml)
hBR96-1
hBR96-2B
hBR96-2C
hBR96-2D
hBR96-2H
hBR96-2A
2B8

FIG.22

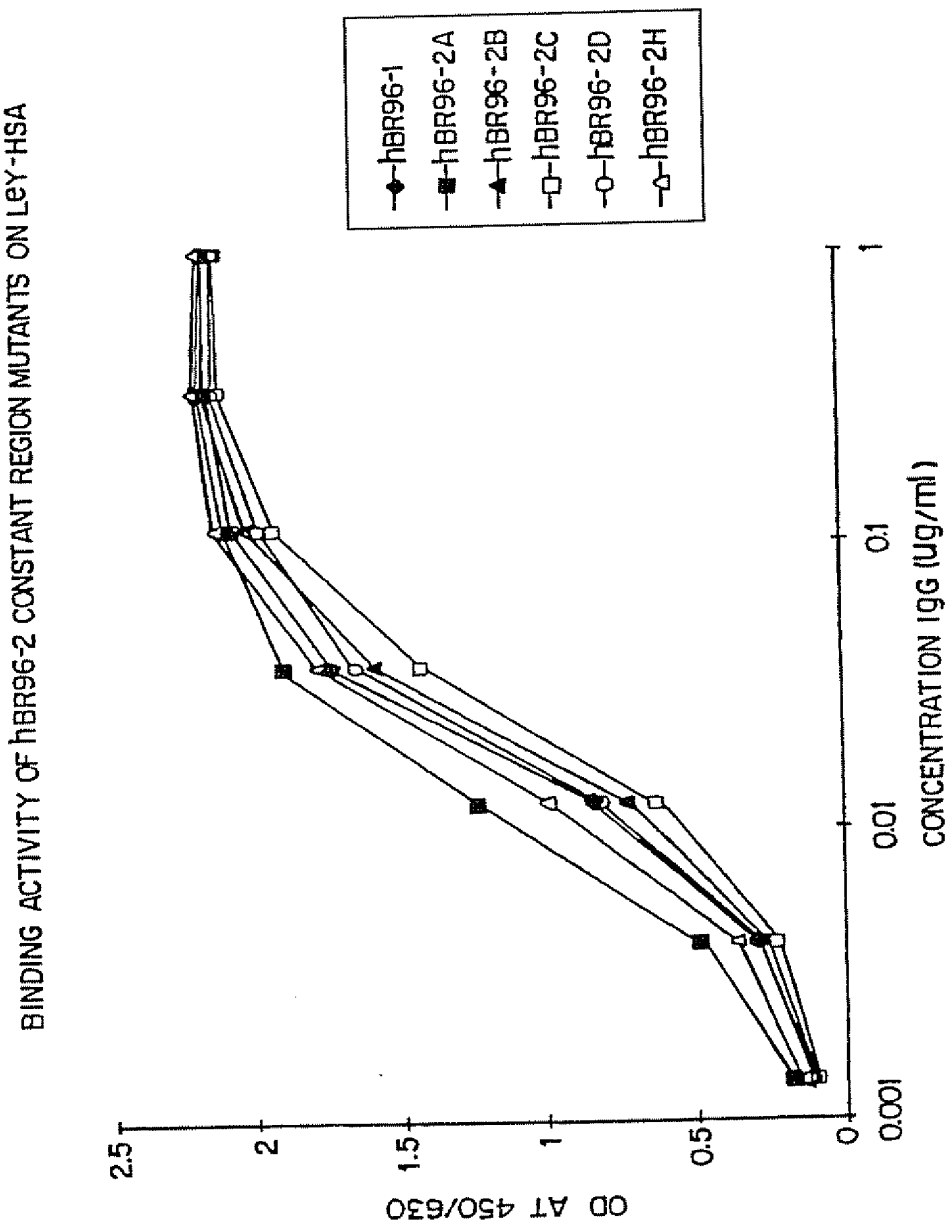
BINDING ACTIVITY OF hBR96-2 CONSTANT REGION MUTANTS ON LeY-HSA
hBR96-1
hBR96-2A
hBR96-2B
hBR96-2C
hBR96-2D
hBR96-2H
OD AT 450/630
2.5
2
1.5
1
0.5
0
0.001
0.01
0.1
1
CONCENTRATION IgG (ug/ml)

FIG.23

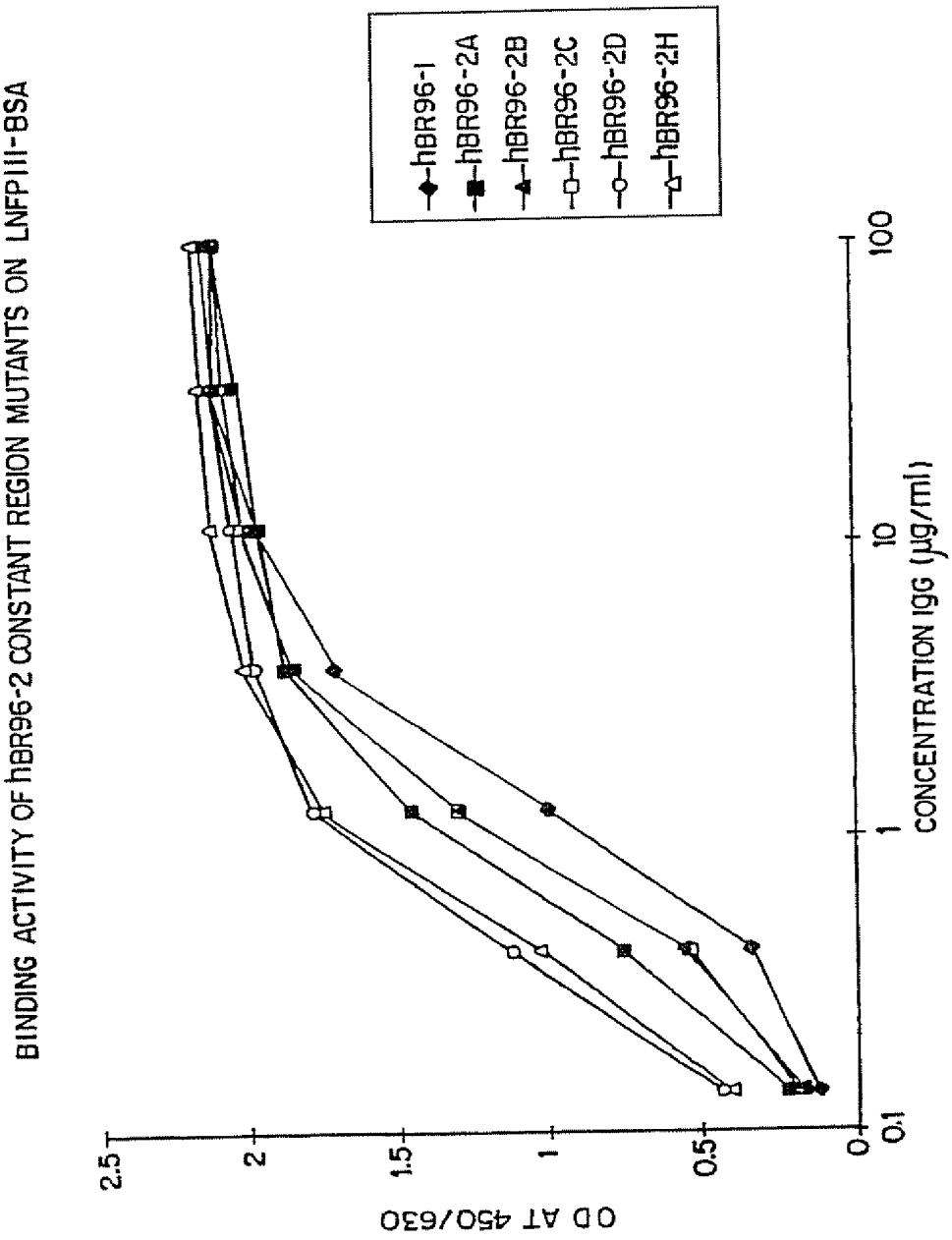
BINDING ACTIVITY OF hBR96-2 CONSTANT REGION MUTANTS ON LNFPIII-BSA
hBR96-1
hBR96-2A
hBR96-2B
hBR96-2C
hBR96-2D
hBR96-2H
OD AT 450/630
2.5
2
1.5
1
0.5
0
0.1
1
10
100
CONCENTRATION IgG (µg/ml)

FIG. 24A

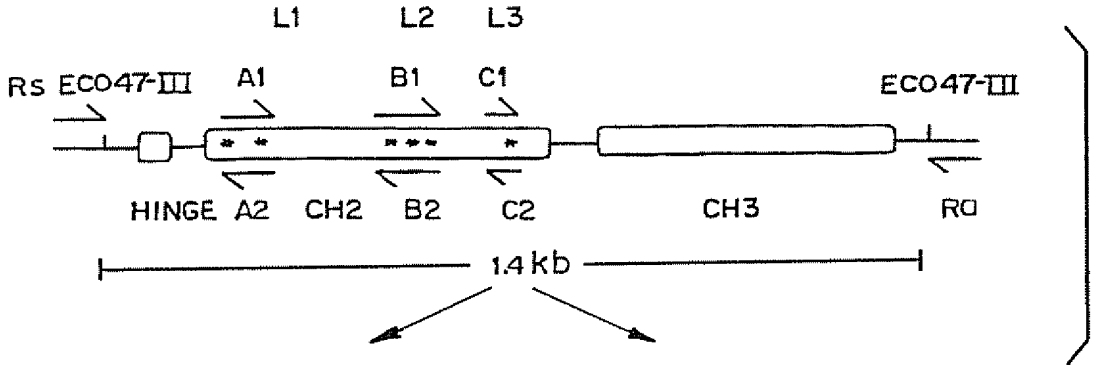

FIG. 24B

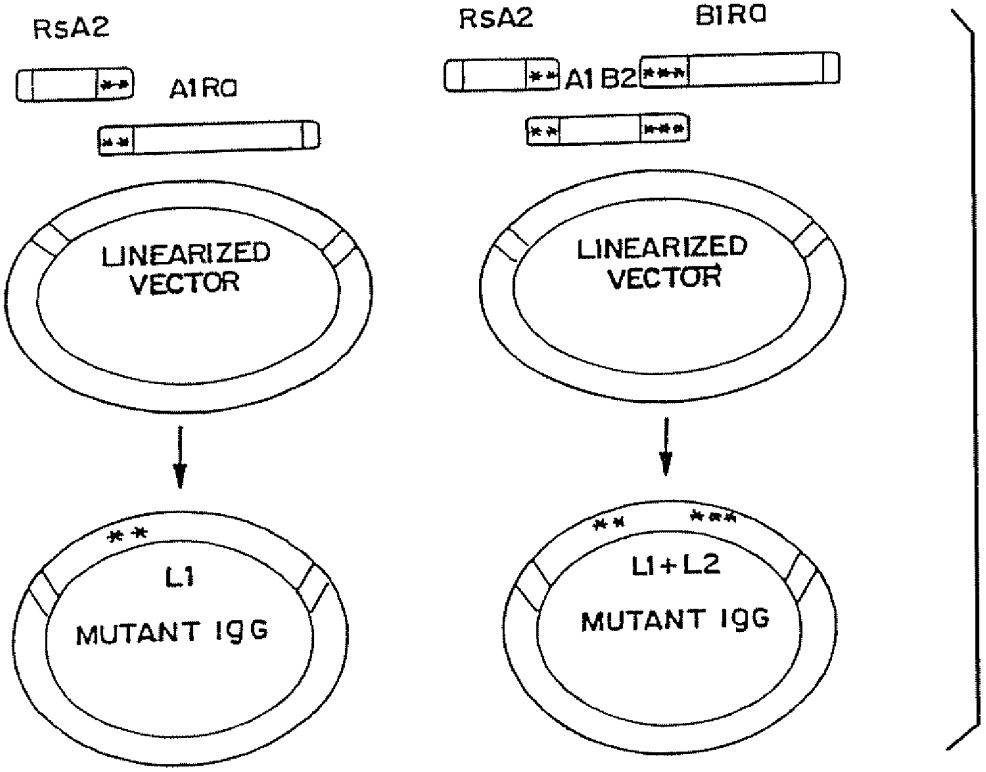

FIG.25

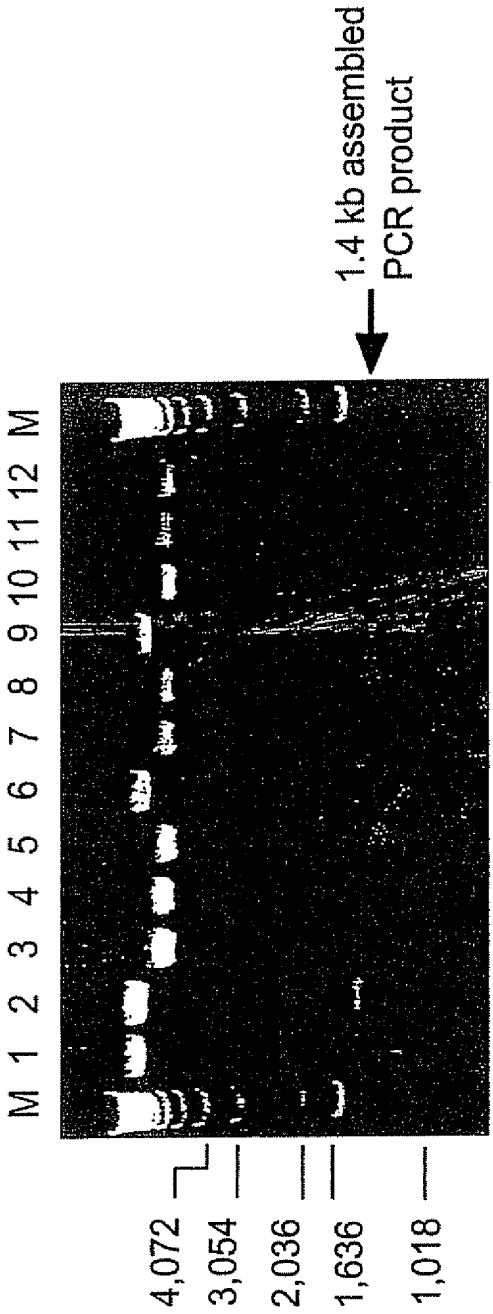
1.4 kb assembled
PCR product
M 1 2 3 4 5 6 7 8 9 10 11 12 M
4,072
3,054
2,036
1,636
1,018

FIG. 26

hBR96-2 Heavy Chain Variable Region (V_H)

(SEQ ID NO:24)

```
1               11              21              31              41
EVQLVESGGG LVQPGGSLRL SCAASGFPFS DYYMYWVRQA PGKGLEWVSY

51          61              71              81              91
ISQDGDITDY ADSVKGRFTI SRDNAKNSLY LQMNSLRDED TAVYYCARGL

101             111
ADGAWFAYWG QGTLVTVSS
```

Human IgG1 Constant

(SEQ ID NO:25)

```
                        CH1
                       A STKGPSVFPL APSSKSTSGG TAALGCLVKD

YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY
                                    CH2 235  237
ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPAPELLGGP SVFLFPPKPK

DTLMISRTPE VTCVVVDVSH EDPEVKFNWY VDGVEVHNAK TKPREEQYNS
                  318 320  322      331          CH3
TYRVVSVLTV LHQDWLNGKE YKDKVSNKAL PAPIEKTISK AKGQPREPQV

YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL

DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK
```

FIG. 27

hBR96-2A: Heavy Chain Variable Region (V_H)

(SEQ ID NO:24)

```
1               11              21              31              41
EVQLVESGGG LVQPGGSLRL SCAASGFPFS DYYMYWVRQA PGKGLEWVSY

51              61              71              81              91
ISQDGDITDY ADSVKGRFTI SRDNAKNSLY LQMNSLRDED TAVYYCARGL

101             111
ADGAWFAYWG QGTLVTVSS
```

hBR96-2A: Human Heavy Chain IgG1 Constant Region ΔCH2

(SEQ ID NO:26)

```
A STKGPSVFPL APSSKSTSGG TAALGCLVKD YFPEPVTVSW NSGALTSGVH
  TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY ICNVNHKPSN TKVDKKVEPK
  SCDKTHTCPP CP    GQPREPQV YTLPPSRDEL TKNQVSLTCL VKGFYPSDIA
  VEWESNGQPE NNYKTTPPVL DSDGSFFLYS KLTVDKSRWQ QGNVFSCSVM
  HEALHNHYTQ KSLSLSPGK
```

FIG. 28

(SEQ ID NO:27)

This sequence is the chi BR96 IgG1 with CH2 deleted.

VH

1 EVNLVESGGG LVQPGGSLKV SCVTSGFTFS DYYMYWVRQT PEKRLEWVAY

51 ISQGGDITDY PDTVKGRFTI SRDNAKNTLY LQMSRLKSED TAMYYCARGL

CH1

101 DDGAWFAYWG QGTLVTVSVA STKGPSVFPL APSSKSTSGG TAALGCLVKD

151 YFPEPVTVSW NSGALTSGVH TFPAVLQSSG LYSLSSVVTV PSSSLGTQTY

CH3

201 ICNVNHKPSN TKVDKKVEPK SCDKTHTCPP CPGQPREPQV YTLPPSRDEL

251 TKNQVSLTCL VKGFYPSDIA VEWESNGQPE NNYKTTPPVL DSDGSFFLYS

301 KLTVDKSRWQ QGNVFSCSVM HEALHNHYTQ KSLSLSPGK